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STUDIES IN THE FREQUENCY, LOCALIZATION, AND MODES OF DISSEMINATION OF TUBERCULOSIS, WITH SPECIAL REFERENCE TO ITS OCCURRENCE IN THE LYMPH NODES AND DURING CHILDHOOD.*

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CONTENTS.

Introduction.
Material.
Methods employed.
Summary of results obtained from autopsies in children.
Latent tubercle bacilli in the lymph nodes.
Tuberculosis in early childhood; congenital tuberculosis.
The main localizations and points of invasion of tuberculosis in childhood.
Frequency of tuberculosis in adults.
The primary localizations of tuberculosis outside of the respiratory tract in adults, with special reference to its occurrence in the lymph nodes and the intestinal tract. The relation of tuberculosis of the lymph glands to pulmonary tuberculosis in adults.

INTRODUCTION.

From November, 1896, to February, 1897, a bill (which later became a law) concerning "measures against tuberculous diseases," drawn up by Holmboe and Klaus Hanssen, was discussed

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106704

in the Medical Society of Christiania. The bill was based mainly on the theory of inhalation as the principal mode of origin of tuberculosis. In the discussion the frequency and the modes and routes of infection were much dwelt upon and opinions varied considerably in regard to the origin of the disease. While some men considered inhalation as the only mode of origin, others advocated infection by way of the intestinal tract as the most frequent source. Dr. Antvord took a special position, based on a thorough investigation of statistics, and claimed that nearly two-thirds of all tuberculous patients contract the disease in childhood, but he gave no further explanation as to how pulmonary tuberculosis of adults originates.

No agreement as to the modes and routes of infection was reached. Personal investigations on a large scale were presented by Dr. J. Bugge, but these concerned only tuberculosis of the lungs and bronchial nodes, mainly in adults. Professor A. Johannessen treated tuberculosis of childhood very thoroughly from the clinical side. Tuberculosis in children from the point of view of morbid anatomy, on the other hand, was not especially considered, although one would expect such a point of view to suggest itself, on account of the greater simplicity of the conditions in children, where, *a priori*, it might be supposed the occurrence and distribution of the disease could be more easily cleared up. Attention would naturally be drawn to the frequency in children of tuberculosis of lymph nodes, especially the cervical nodes—a fact long established by clinical experience.

Some time previously, and while this discussion was going on, I had, as assistant in the Pathological Institute, performed a large number of autopsies upon children. I had noted the frequent, often very extensive, and sometimes even general, tuberculosis of the lymph nodes, and its primary occurrence, especially in relation to pulmonary tuberculosis, in children. In this manner my interest in tuberculosis of childhood was aroused. I therefore decided to give the subject more thorough attention, and I have occupied myself with it ever since, though with many interruptions. In the following years (1898–1900) I performed as many autopsies upon children as possible, with a view to demon-

strate the frequency of tuberculosis in the various groups of lymph nodes. I paid especial attention to the cervical nodes, and, in connection with them, to the tonsils.

During a sojourn in Leipzig in the summer of 1898, I also occupied myself chiefly with this topic, material being kindly given to me from the Pathological Institute of Leipzig by Professor Birch-Hirschfeld, and from the hospital for children conducted by Professor Soltmann (prosector, Dr. Seiffert). However, time only sufficed for the investigation of about 30 autopsies in children.

Having become professor of pathology in the University of Christiania in the summer of 1900, thus securing material of my own, I was enabled to take up these investigations more extensively and to commence a systematic and broader study of the entire subject. It is upon the results of these studies, made from January, 1901, to April, 1904, that my conclusions are mainly based. I shall also, to some extent, consider my earlier investigations (1898–1900) because they help to elucidate certain points in regard to tuberculosis in children, although it is insufficient in other respects to form the basis of conclusions.

I have placed the line between child and adult at the completion of the 15th year. Others, e. g. Nägeli, have placed it at 18, which appears to me rather late, and it is common to place it at 10 or 12. To draw the line at the 15th year, as is perhaps most generally done, seems to me more correct, as in regard to morbid anatomy, the behavior of tuberculosis before and after this age varies considerably, though, naturally, there is no sharp distinction. It is just at and after the 15th year that the transitional forms are seen, lymphatic tuberculosis passing towards the background and becoming superseded by pulmonary tuberculosis in its ordinary adult form. Such a line must, however, necessarily be arbitrary.

It was originally my plan to occupy myself with tuberculosis of childhood only, and especially its primary localizations, with particular reference to the lymph nodes. However, the opportunity to investigate a large number of autopsies in adults has led me to consider those aspects of the occurrence and evolution of

tuberculosis in adults which are directly related to the disease in children. Thus the scope of my work has become much wider, and I trust that in this manner observations of importance have been added. The facts concerning adults over 15 years which I have attempted to elucidate are the following:

1. The frequency of tuberculosis in adults in general, as arrrived at from statistics.

2. Lymphatic tuberculosis in the adult, its frequency, localization, and connection with other tuberculous affections, especially with tuberculous infection in childhood.

3. Primary localizations outside the respiratory tract, especially in the digestive tract.

It is self-evident that all these questions are too broad to be discussed in all their bearings. They are here treated only to the extent suggested by my various observations, and in so far as they have a relation to the main subject, tuberculosis in childhood.

MATERIAL.

My material has been obtained principally from the Pathological Institute, from private autopsies, and from the Municipal Hospital of Christiania. I have, so far as possible, availed myself of accessible literature, but as it is impossible to include everything written on the various aspects of tuberculosis, and as extensive reviews may be found in numerous recent articles, I have considered a complete review of the literature concerned, superfluous. I shall refer principally to the larger recent publications, and to the Scandinavian, particularly the Norwegian, literature, which is relatively little known outside of Scandinavia. Otherwise I shall refer to large collective reviews, such as those of Strauss, Cornet, Hildebrandt, Lubarsch and Ostertag's *Ergebnisse der allg. Path. u. path. Anat.*, Baumgarten's *Jahresberichte*, etc.

METHODS EMPLOYED.

My work has concerned principally the lymph nodes of children. At each autopsy particular attention was directed towards the three chief groups, those of the neck, of the chest, and of the abdomen. In the neck, together with the mucous membrane of

the throat and the tonsils, the superficial and deep groups of nodes, both superior (submaxillary) and inferior (superficial and deep cervical, and supraclavicular), were systematically examined at every autopsy in children. Most frequently changes were observed in the submaxillary nodes. In general the use of the term cervical nodes is meant to signify the submaxillary groups. In the thorax, the nodi bronchiales, nodi hili pulmonares, nodi tracheales, and nodi mediastinales (sometimes also the nodi axillares) were examined. In the literature most frequently the term "bronchial node" is used collectively; here, so far as possible, the special groups have been kept apart. The lungs, of course, were always carefully examined. In the abdomen, the mesenteric nodes were examined (before separation from the intestines); also the retroperitoneal and sometimes the inguinal nodes, and, of course, the entire intestinal tract. At first the investigation was mainly directed to the cervical nodes, the throat and tonsils, especially in the examinations made before 1901. This material, therefore, has been somewhat incompletely elaborated.

The investigations consisted of (1) autopsy with detailed gross examination of the various groups of lymph nodes, (2) inoculations of animals, (3) microscopic examination.

All inoculations were made into guinea pigs. Under aseptic precautions several small nodes or pieces of several large ones were placed under the skin of the right side of the back and the wound sutured. In positive cases swelling and caseation in the nodes of the right groin regularly appeared; afterwards the spleen, liver, and retroperitoneal lymph nodes were attacked, and finally the bronchial and cervical lymph nodes and the lungs. Different guinea pigs were regularly inoculated with material from the cervical, intrathoracic, and mesenteric nodes respectively, whenever swollen nodes could be demonstrated. As a rule the animals were killed after two months. It might be added that only a single case of spontaneous tuberculosis has been observed in our animal barn in the past year.

Microscopic examination was made of the remains of nodes from which inoculations had been made and of neighboring swollen nodes. Nodes from the three chief groups were always

examined and in the largest numbers possible (as a rule from 3 or 4 to 10 or 12). Sections were taken at different levels; serial sections were not made as it would have taken too much time in such an extensive investigation. The microscopic examinations were made as soon as the inoculated animals were killed. In case of positive results, several sections were examined, a number of specimens always being stained for tubercle bacilli.

Occasionally, as recommended by English writers, the fresh juice expressed from swollen lymph nodes was spread upon cover glasses and examined for tubercle bacilli.

It is self-evident that in cases where the autopsy disclosed macroscopic evidences of tuberculosis of the lymph nodes, the examination was confined to the other group of nodes. It is self-evident, too, that the autopsies were conducted with the object also in view of demonstrating tuberculosis in other organs than the lymph nodes.

SUMMARY OF RESULTS OF AUTOPSIES IN CHILDREN.

Before giving my own results I will first briefly review some of the previous statistics concerning tuberculosis in children, with special attention to the publications of last year and to the Scandinavian literature.

An extensive work on tuberculosis in children, mainly of clinical interest, by Abelin[1] appeared in Sweden in 1882. His material was very abundant, comprising 21,932 infants under one year of age, observed from 1842 to 1881, and it has been studied with special reference to miliary tuberculosis. There were 421 deaths from tuberculosis out of a total of 5,410, a mortality of 7.7 per cent from tuberculosis varying from 11.2 per cent to 4.8 per cent in different years. Abelin does not go into details as to the anatomical localizations, though he declares that the bronchial nodes constitute the focus where the "contagion" is at first taken up and from which it spreads.

Medin[2] gives a further analysis of the same material. The 411 deaths deaths from tuberculosis in the first year, detailed information of which was available, were distributed as follows: First month, 5; second, 7; third, 47; fourth, 69; fifth, 82; sixth, 49; seventh, 31; eighth, 30; ninth, 27; tenth, 30; eleventh, 15; twelfth, 16. Ordinary tuberculous meningitis was found in 44 children, and tubercles in the meninges in 23. The points of origin, as a rule, were the lymph nodes and the respiratory tract, more rarely the digestive tract.

The statistics of Biedert[3] include 36,148 children. Of these 1,932 (5.3

[1] *Nord. Med. Arkiv.*, 1882, 14, p. 1.

[2] *Nord. Med. Arkiv.*, 1883, 15, p. 1.

[3] *Jahrb. f. Kinderheilk.*, 1885, 21, p. 158.

per cent) suffered from tuberculosis. Of 1,308 children who died within the first year, 68 per cent had tuberculosis.

The material of Froebelius[1] consisted of 91,370 infants in the St. Petersburg "Findelhaus," 65,680 of whom were ill, with 18,569(?) deaths and also 18,581 autopsies. Among the latter the cause of death was tuberculosis in 416, or four per cent of the total number of infants, 2.2 per cent of the deaths, and 2.5 per cent of the autopsies. Twenty of these died in the first two months, while 396 (95.1 per cent) were two months old or more. (Forty-six, two months; 73, two and one-half months; 54, three months; 55, three and one-half months; 56, four months; 26, four and one-half months; 20, five months; and only 56 six months or more).

In 902 autopsies in children under 15, dead of acute infection, Babes[2] found tuberculosis in 288 (31.9 per cent) and always in the lymph nodes. In 93 autopsies performed in 1887, tuberculosis of the bronchial and mesenteric nodes were present in 65. Death was caused by tuberculosis in only 13 of these cases.

From Denmark we have two valuable publications by Geill[3] on lymphatic tuberculosis in children, its frequency and seat (1888 and 1890). Of 902 autopsies in children under 15, dead from acute infections, he found tuberculosis in 288 (31.9 per cent) distributed as follows:

Under three years	430 autopsies	89 cases	(20.7%)
3–6 years	334 "	139 "	(41.6%)
6–9 "	98 "	46 "	(46.9%)
9–12 "	35 "	14 "	(40%)
12–15 "	5 "	0 "	

Monrad[4] reports finding tuberculosis in 157 out of 654 autopsies in children (only five cases were latent). In the first year 9.2 per cent of the cases (33 of 356) were tuberculous; in the second year 32 per cent; third to fifth year 46.9 per cent, and fifth to fifteenth year 49.4 per cent.

The work of Müller[5] is important. In 500 autopsies on children in the Munich Pathological Institute death was due to tuberculosis in 150 (30 per cent), and 59 (11.8 per cent) had latent tuberculosis which most commonly was virulent, rarely obsolete.

Hecker's[6] work is a continuation of Müller's statistics. In 700 autopsies in children tuberculosis was the cause of death in 97 (13.9 per cent), and latent tuberculosis was present in 50; hence a total of 147 (21 per cent) with tuberculosis infection. Combining the two sets of statistics we get a mortality of 20.5 per cent. According to the figures of Müller tuberculosis was rare in the first year and then rapidly increased, 41.3 per cent of all cases occurring between the first and fourth year, then decreased, and again increased between 13 and 15. Müller mentions three cases dying in the first year, at twelve, eight,

[1] *Jahrb. f. Kinderheilk.*, 1886, 24, p. 47.

[2] Quoted from BAUMGARTEN'S *Jahresberichte.*

[3] GEILL, C., *Hosp.-Tid.*, 1888, 3 R., 6, pp. 249, 278; *Bibliothek f. laeger*, 7 R., 1890, 1, p. 725.

[4] *Hosp.-Tid.*, 1902, 10, p. 300.

[5] *Zur Kentniss der Kindertuberkulose.* Inaugural Dissertation, 1890.

[6] *Münch. med. Wchnschr.*, 1894, 40, p. 391.

and four months respectively. Hecker 10 cases, one under three months; three, three to six months; and six, six to 12 months old.

From the Pathological Institute of Kiel (Professor Heller) statistics have been published by Schwer, Simmonds, and Boltz.[1]

Schwer:	728	autopsies	in	children.	Death	from	tuberculosis	in 17 %
Simmonds:	576	"	"	"	"	"	"	" 21.6%
Boltz:	1,272	"	"	"	"	"	"	" 13.8%
Total:	2,572	"	"	"	"	"	"	" 16.7%

Of Boltz's 1,272 cases 153 were stillborn and 201 less than four weeks old. None of these died of tuberculosis. Between five and 10 weeks one child died of tuberculosis (which was about one per cent of the total deaths at that age). Between three and five months 8.6 per cent died of tuberculosis; 12 months 8.3 per cent; one to two years 26.8 per cent; two to three years 33 per cent; three to four years 29.6 per cent; four to five years 31.8 per cent; five to 10 years 34.3 per cent; 10 to 15 years 30 per cent. In 1,430 autopsies in children under one year 64 (4.5 per cent) were found to be tuberculous; in 781 one to five years old 230 (29.3 per cent); in 228 five to 10 years 78 (35 per cent); in 162, 10 to 15 years 56 (34.6 per cent).

From later statistics by Heller[2] we learn that in 714 children dead of diphtheria latent tuberculosis was found in 140 (19.6 per cent). A recent collective report from Kiel by Hof[3] shows that 936 (20.1 per cent) of 4,649 children which came to autopsy were tuberculous.

Nebelthau[4] in 1903 collected the material from 17 statistics and found that in 8,770 autopsies in children tuberculosis had been found in 1,796 (20.4 per cent).

In 806 autopsies in children reported by Baginsky[5] tuberculosis existed in 144 (17.8 per cent).

H. Schmidt[6] collected the material from the Pathological Institute of Erlangen for the years 1863 to 1895 and found tuberculosis as the cause of death in 325 children under 10 years, 23 per cent of the total number of this age. In 11 additional cases latent tuberculosis was found.

Racynskyi[7] found a very similar percentage. Of 12,152 children treated in the stationary clinic of St. Ludwig's Hospital for children in Cracow, 3,341 died, 611 (18.3 per cent) of tuberculosis. In the 2,720 other autopsies latent tuberculosis was found in 112 or 4.1 per cent, a strikingly small number. Of 828 who died under one year of age 74 (8.8 per cent) died of tuberculosis; of 624 one to two years 123; of 419 two to three years 118; of 627 three to five years, 126; of 453, five and two years, 125; and of 260, eight and 12 years, 45 died of tuberculosis.

[1] *Ein Beitrag zur Kindertuberkulose.* Inaugural Dissertation, 1890.

[2] *Münch. med. Wchnschr.*, 1902, 49, p. 609.

[3] *Ueber primäre Darmtuberculose nach 15000 Sectionen.* Inaugural Dissertation, 1903.

[4] *Münch. med. Wchnschr.*, 1903, 50, pp. 1246; 1300.

[5] *Deutsche med. Wchnschr.*, 1902, 28, (Vereinsbeil.), p. 270.

[6] *Ueber die Häufigkeit der Tuberkulose in den verschiedenen Lebensaltern.* Inaugural Dissertation, 1897.

[7] *Jahrb. f. Kinderheilk.*, 3. F., 1901, 4, p. 67.

Kossel[1] has given an important contribution. Of 286 children under 12, 36 (12.6 per cent) had tuberculosis. The disease was latent in 14 of these cases (all over one and one half year) while 22 had died of tuberculosis. Of 226 under one year 14 (six per cent) died of tuberculosis. Of 60 over one year eight died of tuberculosis while fourteen had latent foci. Of 59 children suffering from other diseases 28 (40 per cent) reacted to tuberculosis (*i. e.*, they had latent tuberculosis).

Nägeli[2] found 15 cases of tuberculosis (17 per cent) in 88 autopsies in children. There were 35 autopsies with six cases of tuberculosis (17 per cent) at the ages of one to five years, 33 per cent tuberculosis at five to nine years, 38.7 per cent at nine to 17 years.

In Norway an extensive statistical work by J. Bugge[3] has appeared. This is of special interest as it only includes cases examined by himself, and because microscopic examination and animal inoculations quite frequently were employed. However, his autopsies in children are comparatively few. Of 21 under one year one had tuberculosis; of 22 between one and nine years 15 (68 per cent), 12 of these fatal, three latent; of 18 between 10 and 19 years (most of them over 15), 16 (89 per cent) had tuberculosis (six died of it, six had latent virulent foci). Hence, in the bodies of 61 persons under 19 years of age tuberculous changes were found in 32 (over 50 per cent).

Various statistics are also found in the English literature. Thus Still[4] in 769 autopsies in children under 12 years found 269 cases of tuberculosis (35 per cent); 43 of the cases were latent; 117 cases (43.4 per cent) occurred before the second year.

In America Hand[5] found 115 cases (34.6 per cent of tuberculosis in 332 autopsies in children. Councilman, Mallory, and Pearce[6] in 220 children dead of diphtheria found latent tuberculosis in 35 (16 per cent). Cohaus[7] in 459 children likewise dead of diphtheria (from Kiel) reports 95 cases of tuberculosis (20.7 per cent), Cronemeyer[8] 60 out of 459 (13.3 per cent).

In a recent discussion in the Berliner medizinischen Gesellschaft, Orth[9] gave his experiences from the Charité for the preceding 15 months. Of 1,558 autopsies 287 were in children under one year. Ten of these (3.4 per cent) had tuberculosis; of 131 cases between the ages of one and 15 years 37 (28 per cent) had tuberculosis, *i. e.*, about 11 per cent tuberculosis in all autopsies in children. In the same discussion Baginsky[10] related that he had observed 1,383 cases of tuberculosis in children, 245 of which (17.2 per cent) occurred in the first year: first month, two; second, seven; third, 23; fourth,

[1] *Ztschr. f. Hyg. u. Infektionskr.*, 1896, 21, p. 59.

[2] *Virch. Arch.*, 1900, 160, p. 426.

[3] *Undersögelser om Lungetuberkulosens Hyppighed og Helbredelighed.* Christiania, 1896.

[4] *Brit. Med. Jour.*, August 19, 1899, 2, p. 755.

[5] *Proc. Path. Soc., Phila.*, 1903, 6, p. 132. Also *Arch. Pediat.*, 1903, 20, p. 427.

[6] *Jour. of the Bost. Soc. of Med. Sci.*, 1900, 5, p. 139.

[7] Cited by COUNCILMAN, MALLORY, and PEARCE.

[8] Cited by COUNCILMAN, MALLORY, and PEARCE

[9] *Berl. Klin. Wchnschr.*, 1904, 41, p. 265.

[10] *Verh. d. Berlin. med. Gesellsch.*, February 10, 1904.

15; fifth, 30; sixth, 34 etc.). Lubarsch[1] states that in 297 autopsies in children under 15 years tuberculosis was found in 63 cases (21.2 per cent).

We come now to my own investigations. At first the results of my work in Leipzig in the summer 1898 will be given. Thirty children came to autopsy; microscopic examinations were made, mainly of the lymph nodes, and especially of the cervical group. Tuberculosis was demonstrated in nine (30 per cent); in five of these as the cause of death (ages eight months, one and one-half, one and one-half, two and one-fourth, and four and one-half years respectively), while in the other four cases it was an accidental finding, in two (six and three-fourths and eight years old) exclusively in the bronchial and hilus nodes and demonstrable macroscopically, in the other two only microscopically (in the one child in the mucous membrane of the throat and cervical nodes, in the other both in the cervical and hilus nodes).

Of the five children dead of tuberculosis, in three the starting point was in the intrathoracic nodes and in the lungs; in the other two there was an almost universal lymphatic tuberculosis which in one of the cases seemed to have commenced in the cervical nodes. In the other 21 children (70 per cent), 11 of whom died in the first year, six in the second, three in the third, and one six and one-half years old, there was no evidence of tuberculosis; in all of them the cervical nodes were examined microscopically, in most of them also the bronchial nodes, but only in about one-fourth the mesenteric nodes. Inoculations in guinea pigs, on the other hand, were not made; for that reason these cases have not been included in the tables to be given later.

As to the investigations made at the pathological institute in Christiania, I shall group those made in 1898–1900 separately as Series I (partly incompletely studied); those made between January, 1901, and February, 1904, and completely worked up, as Series II.[2]

[1] *Fortschr. d. Med.*, 1904, 22, p. 701.

[2] The details of each case cannot be given here, but will be found in my work: "Studien über die Häufigkeit, Lokalisation und Ausbreitungswege der Tuberkulose, insbesondere mit Berücksichtigung ihres Sitzes in den Lymphdrüsen und ihres Vorkommens im Kindesalter." *Forh. af Videnskabsselskabet i Christiania*, 1904 (math.-naturvid klasse, No. 8).

In the years 1898–1900 (Series I) 133 children under 15 years came to autopsy. Forty-eight of these (36.1 per cent) were infected with tuberculosis, 85 (63.9 per cent) were free from macroscopic signs of the disease; and inoculations in guinea pigs with lymph nodes, tonsils, etc., gave negative results, as did microscopic examinations whenever made.

In the years 1901–April 1904 (Series II) there were 142 autopsies in children under 15 years. In 69 cases (48.6 per cent) tuberculous infection existed, while in 73 cases (51.4 per cent) no tuberculous changes were found, and inoculations from them were negative. Hence, the number of infected cases is greater in this series, principally because in many cases latent lesions existed which were only revealed by inoculations or microscopic examination.

Combining the two series we have 275 autopsies in children, in 158 of which, *i. e.*, 57.5 per cent, no tuberculous lesions or tubercle bacilli were found, while they were present in 117, or 42.5 per cent.

It will be noted that these figures are very high, especially those of Series II in which nearly half the cases show tuberculous infection, and even if we only consider the total figure of 42.5 per cent they exceed those in nearly all the statistics previously mentioned, in most of which the percentage was in the neighborhood of 20 (Monrad, 24; Hecker, 21; Schwer, Simmonds, and Boltz, 16.4; Baginsky, 17.8; the series from Kiel, 20.1; Nebelthau, 20.4; H. Schmidt, 23; Racynskyi, 22.4; Kossel, 12.6; Nägeli, 17; Orth, 11; Lubarsch, 21.2). Several authors, however, give figures from 30 to 35 per cent.—Babes, 31.9; Geill, 31.9; Müller, 41.8; Still, 35; Hand 34.1.

It is of interest that Bugge, whose material also came from the pathological institute of Christiania, likewise found a high percentage, over 50 per cent. However, his 61 autopsies also included cases between 15 and 19 years of age. He also made thorough microscopic examinations.

The objection might be raised that the high percentages could be accounted for by the source of our material, but the state hospital in Christiania ("Rigshospitalet") from which most of

our material was obtained, admits all classes of patients, and preferably non-tuberculous cases. This is particularly true of the pediatric wards. Private and medicolegal cases were also included in order to avoid any kind of selection. The high figures are not only due to the many fatal cases, but also to a large number in which the presence of latent tubercle bacilli was revealed by animal inoculations. It will also be noticed that numerous instances of tuberculous infection were met with in the large number of children less than one year or even only a few months old which I examined. This is shown by the succeeding tables of autopsies of tuberculous and non-tuberculous children.

TABLE I.

NON-TUBERCULOUS CHILDREN.

	Series I 1898-1900		Series II 1901-April 1904		Total	
0- 3 months	22	42 in first year	25	56 in first year	47	78 in first year
4- 6 "	14		12		26	
7- 9 "	2		11		13	
10-12 "	4		8		12	
1- 2 years	21		10		31	
2- 3 "	6		0		6	
3- 4 "	4		2		6	
4- 5 "	1		0		1	
5- 6 "	0		0		0	
6- 7 "	2		1		3	
7- 8 "	2		1		3	
8- 9 "	2		0		2	
9-10 "	0		1		1	
10-11 "	1		0		1	
11-12 "	0		1		1	
12-13 "	0		1		1	
13-14 "	1		0		1	
14-15 "	3		0		3	
	85		73		158	

It is seen that most of the non-tuberculous children were under two years of age, two-thirds of them even under one year.

In the following table of tuberculous cases latent or obsolete tuberculosis is placed separately, and in Series II also cases in which latent bacilli were demonstrated by inoculations.

TABLE II.

TUBERCULOUS CHILDREN.

	SERIES I—1898-90		SERIES II—1901-APRIL 1904			TOTAL
	Died	Latent and Obsolete Tuberculosis	Died	Latent and Obsolete Tuberculosis	Latent Bacilli	
0- 3 months.....	3 } 7 in	..	1	..	2 } 18 in	6
4- 6 "	0 } first	..	4	..	3 } first	7
7- 9 "	2 } year	..	0	1	3 } year	6
10-12 "	2	..	2	1	1	6
1- 2 years.....	4	..	5	..	2	11
2- 3 "	1	..	1	1	3	6
3- 4 "	2	..	..	1	..	3
4- 5 "	3	..	2	..	..	5
5- 6 "	3	..	3	1	..	7
6- 7 "	1	..	1	..	2	4
7- 8 "	5	1	..	1	1	8
8- 9 "	0	1	..	..	..	1
9-10 "	1	1	1	1	..	4
10-11 "	4	2	2	2	1	11
11-12 "	2	..	1	1	..	4
12-13 "	0	3	1	1	..	5
13-14 "	2	1	1	..	..	4
14-15 "	4	..	8	7	..	15
	39	9	33	18	18	117
	48		69			

To summarize: Of 117 tuberculous cases 72 or 61.5 per cent died of tuberculosis; 21 cases (23 per cent) had latent or obsolete tuberculous lesions, while in 18 cases (15.3 per cent) latent tubercle bacilli existed. As before stated, the percentages in Series I probably are too small as seen by comparison with those of Series II. Nevertheless, it may be of interest to compare Tables I and II. After the fourth year the tuberculous cases are seen to predominate over the non-tuberculous ones, and in increasing ratio. Thus, among the 22 children between 14 and 15 years old, 19 had tuberculosis.

On the other hand, if we compare those under four years, most of them are seen to be without tuberculous infection, and here also the relative frequency increases with the age. This progressive increase becomes very plain if we compare conditions in the quarters of the first year, with only 11.3 per cent of tuber-

culous cases in the first quarter, 21 per cent in the second, etc., constituting a good argument against the frequency of congenital tuberculosis, and being in accord with the findings in most other statistics.

TABLE III.

FINDINGS IN CHILDREN UNDER FOUR YEARS OF AGE.

Age	Number of Non-tuberculous Cases		Number of Tuberculous Cases		Total Number Examined
0– 3 months.....	47	98	6	25	123
4– 6 "	26		7		
7– 9 "	13		6		
10–12 "	12		6		
1– 2 years.....	31		11		42
2– 3 "	6		6		12
3– 4 "	6		3		9
4–15 "	17		72		89

However, the number of tuberculous cases in the first year (in 25 of 123 autopsies) is large as compared with the statistics of others. In addition to the 14 fatal cases (four, four, two, and four cases per quarter respectively), it is noteworthy that two cases of latent tuberculosis occurred at this age, and the fact deserves special emphasis that in no less than nine cases in the first year latent tubercle bacilli were demonstrated, while two such cases occurred in the second year and three in the third year. This will be further discussed later.

The statistics of other writers, with much smaller proportion of tuberculosis in the first year, are generally based on heterogeneous material collected from long periods and by different prosectors, without any special effort having been made to demonstrate a tuberculous infection; mention is not made of microscopic examination and of inoculations. Thus Monrad in children under one year of age found tuberculosis in 9.2 per cent (in the second year in 32 per cent), Boltz in 4.5 per cent (from one to five years 29.3 per cent), Racynskyi in 8.8 per cent (in the second year in about one-sixth, third year one-third to one-fourth etc.), Kossel, in six per cent (but in children over one year in 36 per cent), Orth in 3.4 per cent (but in children from one to 15 in 28 per cent). Baginsky noted the frequent

occurrence of tuberculosis in infants a few months old but does not give the percentage at different ages; Abelin in 7.7 per cent, Froebelius in 2.5 per cent of infants.

The cases of latent and obsolete tuberculosis were relatively few, being 27 in our two series combined, or in 9.8 per cent of the 275 autopsies performed, or in 23 per cent of the total 117 tuberculous cases. The number is also small compared to the number of cases in which tuberculosis was the cause of death (72), and particularly small when compared to the 18 cases in which latent bacilli were found. The reason may partly be in the nature of the material which included very few cases of contagious diseases, in which (measles, diphtheria etc.) experience seems to show that latent tuberculosis is most frequent (Babes 31.9 per cent, Müller 11.8 per cent, Kossel 40 per cent, Heller 19.6 per cent, Councilman, Mallory, and Pierce 16 per cent, Cohaus 20.7 per cent, Cronemeyer 13.3 per cent etc.). Another reason lies in the fact that so many of the children in this series had died during the first year in which latent and obsolete forms are known to be rare.

The latent and obsolete tuberculosis was most frequently located in lymph nodes which were caseous, and partly in the lungs, in the latter case, as a rule, together with changes in the thoracic lymph nodes. The lymph nodes within the thorax were found to be infected most frequently (25 times), the cervical nodes and tonsils nine times, and the mesenteric nodes seven times.

Most frequently the diagnosis of tuberculosis could be made macroscopically. However in 12 cases it could only be made after microscopic examination.[1] Thus, in a girl nine years old, fibrous and hyalin tubercles were found in the bronchial nodes. In a girl, 14 years old, with caseous tracheal and bronchial nodes the cervical nodes on histological examination were found tuberculous, and positive results were obtained by inoculations from enlarged mesenteric and retroperitoneal nodes. In a girl, 12 years old, who died of a fracture of the femur, all groups of lymph nodes were somewhat enlarged; histologically, fibrous and

[1] The same was true of two of the nine tuberculous cases in the 30 Leipzig autopsies.

hyalin tubercles and hyalin degeneration were demonstrated in the cervical, bronchial, mediastinal and mesenteric nodes. In a child, four years old, dead of joint and miliary tuberculosis, tubercles were found in enlarged cervical nodes and in the tonsils. The tubercles were partly recent and of usual appearance, partly fibrous and hyalin, and an extensive hyalin degeneration in other parts of the parenchyma indicated a marked regressive tendency of the disease in these nodes. In a boy, 10 years old, all nodes, especially in the cervical group, were enlarged. Negative results were obtained by inoculations from the cervical nodes, but all nodes examined presented extensive hyalin degeneration, and fibrous and hyalin tubercles of typical structure, *i. e.*, a general lymphatic tuberculosis had almost passed away.

On the whole hyalin degeneration in lymph nodes always creates a suspicion of tuberculosis and is a valuable guide in the histological examination. On the other hand, I have not found the so-called large-celled hyperplasia in lymph nodes to be indicative of tuberculosis except in the presence of distinct tubercles. I find no reason to enter into other microscopic details.

Along with the twelve cases where microscopic examination only revealed tuberculosis of the lymph nodes we have numerous and extensive microscopic examinations with negative results, as shown in our series of non-tuberculous children. In 54 of the 73 cases (Series II) with negative gross finding microscopic examination was made of the cervical nodes and tonsils (in 52 cases), of the tracheobronchial nodes (in 27 cases) and of the mesenteric nodes (in 30 cases)—with negative results in all. In 37 of these cases inoculations of guinea pigs were also made and with negative results.

LATENT TUBERCLE BACILLI IN THE LYMPH NODES.

We now come to an important point where my investigations have brought positive results in a direction to which hitherto little attention has been given, namely, *the occurrence in lymph nodes of tubercle bacilli demonstrable by inoculation, without concurrent macroscopic or microscopic changes.*

What do we find in medical literature concerning this subject?

Information is as yet scarce, especially as to autopsies in children, though it appears that recently more attention has been given to the subject. The most important of these investigations, some of which also concern adults, are the following:

Loomis[1] made intrapleural inoculations in rabbits of material from the bronchial nodes of 30 adult bodies free from macroscopic tuberculosis. He claims positive results in eight cases (plus three uncertain ones), but the results are not very convincing as several of the animals are said to have died in 10 or 15 days. The nodes were not examined microscopically.

Nor are Pizzini's[2] experiments unassailable though generally accepted as correct. He inoculated rabbits intraperitoneally and subcutaneously with material from the bronchial, mesenteric, and cervical nodes of 40 adult bodies. In 10 cases the animals died of peritonitis or septicemia. Of the animals inoculated from the remaining 30 cases 11 became tuberculous. In all successful inoculations bronchial nodes had been used, in one also cervical nodes, while no positive results were obtained from the mesenteric nodes. Only four cases (Nos. 9, 10, 22, and 29) are unobjectionable, while in the others the animals died of tuberculosis so early and with such severe changes that doubt is thrown on the reliability of the experiments.

Spengler[3] examined macroscopically and microscopically the bronchial nodes of six children one-half to nine years old. In all cases he found tubercle bacilli in cover glass preparations from the nodes even in cases without gross or microscopic evidence of tuberculosis. Inoculations were not made. The mesenteric and cervical nodes were similarly examined, with negative results.

Perez[4] on the basis of animal experiments, claims that tubercle bacil may remain latent in lymph nodes, and that they rapidly lose their virulence and only give rise to a mild infection. Tubercle bacilli, injected subcutaneously, soon disappeared from the blood and viscera but remained for months in the lymph nodes from which they could be obtained in pure culture. They had lost their virulence.

The interesting experimental research of Manfredi and B. Frisco[5] deals with the latency of microbes in lymph nodes and their immunizing effect. They showed that this latency of microorganisms in lymph nodes is frequent and generally harmless, but may be the starting point of a "cryptogenic infection" of the body, that the virulence of the organisms decreases and an immunizing effect is exerted on the body. They also showed that tubercle bacilli may penetrate the skin or mucous membranes without producing lesions in them, to be retained in the lymph nodes and remain alive a certain time (three to four months). There they undergo a form of granular degeneration and gradually lose their virulence. According to the number and virulence of the bacilli and the power of reaction of the lymph nodes the result is either

[1] *Jour. Am. Med. Assn.*, 1891, 16, p. 98; abstract in *Deutsche med. Wchnschr.*, 1892, 18, p. 756; quoted by Pizzini (*loc. cit.*)

[2] *Ztschr. f. klin. Med.* 1892, 21, p. 329.

[3] *Ztschr. f. Hyg. u. Infectionskr.*, 1893, 13, p. 347.

[4] *Centralbl. f. Bakt.*, 1898, 23, p. 404. [5] *Centralbl. f. Bakt.*, 1902-03, *Refer*, 32, p. 295.

a mere latent scanty deposit of bacilli, without specific histological changes, or a local eruption of tubercles, or a general infection.

Kälble[1] injected guinea pigs intraperitoneally with emulsions in sterile broth of bronchial nodes from bodies without gross or microscopic tuberculous lesions. Of the 23 animals which did not succumb to suppurative peritonitis two became tuberculous. It was concluded that in these two cases the glands had contained virulent tubercle bacilli without presenting demonstrable changes (one was a man of 41, the other a child of five and one-half years.)

The observations of Walsham[2] are less important. He demonstrated microscopically tubercle bacilli in the bronchial and cervical nodes obtained from autopsies in 26 tuberculous adults and children, and maintains that in about one-fourth of the cases tuberculous infection cannot be recognized merely by the histologic picture, among other reasons because a really tuberculous large-celled hyperplasia readily might be misinterpreted.

The best and weightiest contribution to the study of the occurrence of latent bacilli in lymph nodes is a recent one by Allan Macfadyen and Alfred MacConkey.[3] These observers injected subcutaneously and intraperitoneally in guinea pigs the crushed mesenteric nodes from the bodies of 28 children. The animals were killed after six to eight weeks. Only two of the children were over five years. Eight had various tuberculous lesions. Of the remaining 20 cases positive results were obtained in five, one a still-born infant, the others six months, six months, two and one-fourth years, and eight years old respectively.[4] In two of these cases tuberculosis was present histologically so latent bacilli were really only demonstrated in three (or two) cases. The same authors in a similar manner examined the adenoid vegetations of 44 children, and the tonsils of 34, all with negative result.

In my Series II[5] of 142 autopsies it will be remembered that latent tubercle bacilli were demonstrated in 18 of the 91 cases in which there was no gross nor histological sign of tuberculosis. As stated, no tubercles or tuberculous granulation tissue could be found by painstaking histological examination of the nodes and other parts of the body in these cases.

The objection might be raised that as the nodes used in the inoculations could not also be examined histologically, microscopic lesions might have existed. If so, not only latent tubercle bacilli, but also real latent tuberculosis, would have been present,

[1] *Münch. med. Wchnschr.*, 1899, 46, p. 622.

[2] *Jour. of Path. and Bact.*, 1901, 7, p. 409.

[3] *Brit. Med. Jour.*, July 18, 1903, 1, p. 123.

[4] As to the still-born infant it is also stated that the result of the inoculation from the mesenteric nodes was negative.

[5] Series I cannot be used in this connection on account of the small number of inoculations made.

and the existence of virulent bacilli be of less interest.[1] However, this explanation is hardly correct when we consider the large number of successful inoculations and the thorough histological examination made of adjacent nodes of the same groups. It would be strange if tubercles, if present, would not have been discovered in at least a few of the nodes examined. The mere macroscopic examination by an experienced pathologist is also of great value, though, of course, far from sufficient.

On the other hand, this objection may justly be raised against many of the series of experiments mentioned where inoculations only, and no histological examinations, had been made (see the investigations of Macfadyen and MacConkey).

In order to attempt to demonstrate such latent tubercle bacilli in apparently normal tissue, I have also examined for tubercle bacilli sections from nodes adjacent to those from which successful inoculations were made. Chances were naturally small on account of the probably small number of bacilli present. I have made such controls in 10 cases, with negative result. Bacilli were never demonstrated with certainty; only red granules and rod-shaped bodies.

In these examinations attention was also directed to the so-called "capsules of Schrön," "Keimprodukten" of tubercle bacilli, which d'Arrigo[2] claims to have seen in scrofulous nodes, which findings, however, hardly have met with general recognition. Walsham, however, has demonstrated such involution forms in caseous nodes. But no such globular or oval bodies, which d'Arrigo describes and believes to be products of tubercle bacilli, could be demonstrated.

Perhaps latent tubercle bacilli might have been demonstrated in still more cases if search had been made in cover glass preparations made from the expressed juice, a method apparently successfully employed by several earlier observers (see Spengler, Walsham), but which I have tried only a few times. By this

[1] This objection has been strongly raised against the work of Loomis and Pizzini by Bugge (*loc. cit.*, pp. 50-51), who also has shown that in a node which shows no gross evidence of tuberculosis the disease may be demonstrated by histological examination of one-half of it, and inoculation of the other half give positive result.

[2] *Centralbl. f. Bakt.* I. 1900, 28, p. 481.

method one should be enabled to examine a larger quantity of tissue, and it ought to be borne in mind in future investigations:

It is of great interest to note the age of the children in which latent bacilli were detected, and the groups of nodes from which successful inoculations were made. Both will be shown in the following tables:

TABLE IV.

NUMBER OF CASES SHOWING LATENT BACILLI AT DIFFERENT AGES.

0– 3 months	2	10
4– 6 months	2	
7– 9 months	5	
10–12 months	1	
2d year	3	
3d year	2	
6th year	1	
7th year	1	
11th year	1	
Total	18	

TABLE V.

NODES GIVING VIRULENT BACILLI ON INOCULATION.

Cases from Series II	Age	Nodes
1	2¾ years	Cervical nodes
2	2 years	" "
3	7½ months	" "
4	10 years	" "
5	2½ years	" "
6	14 months	" "
7	3½ months	" "
8	4 months	" "
9	2 months	" "
10	6½ months	Cervical and mesenteric nodes
11	6 months	Cervical nodes
12	5 years	Mesenteric and retroperitoneal nodes
13	9½ months	Cervical nodes
14	1 year	Cervical and tracheal nodes
15	52 days	Tracheal nodes
16	6 months	Cervical, tracheal, and mesenteric nodes
17	6 years	Cervical nodes
18	8 months	" "

It is a striking fact that virulent bacilli were demonstrated most commonly in very young children who also formed the bulk of the autopsy material. Not less than 10 of the 18 cases were in children less than one year of age, three were between

two and three years, and only three over three years. By comparison it will be recalled that of the 73 non-tuberculous children, 56 were less than one year old (25, 12, 11, and 5 in each quarter) and 10 between one and two years; as will also be remembered, the lymph nodes were examined microscopically in 54 cases and inoculations made 37 times.

It is also a noteworthy fact that virulent tubercle bacilli, as a rule, only have been demonstrated in certain groups of lymph nodes, oftenest in the cervical nodes. Thus, the cervical nodes gave positive result in not less than 13 cases, to which one case must be added in which both the cervical and mesenteric nodes gave positive results, and also one with positive results from the cervical, tracheal, and mesenteric nodes. However, it must be borne in mind that in the beginning the work, both as regards inoculations and histological examination, attention was especially directed to the cervical nodes.

Another reason for the selection was the fact that these nodes most commonly were enlarged and thus invited further investigation. In the 73 cases with negative findings the cervical nodes were examined histologically in 52 cases and inoculations from these nodes and the tonsils were made in 34 cases.

In the mesenteric nodes bacilli were found in only three cases; namely, in these nodes alone in one case, together with the cervical nodes in one, and with the cervical and tracheal in one (in a child six months old). This is a small number, and probably too small, as until the middle of 1902 observation was not sufficiently directed toward these nodes, and relatively few inoculations were made from them. It should, however, be remembered that in 21 of the 73 non-tuberculous cases inoculations from the mesenteric nodes had been made and with negative result. Future investigations might advantageously be specially directed to these nodes,[1] the more so as the address of v. Behring on the routes of infection has caused more attention to be given to the digestive tract in recent discussions, and because many facts point to this tract being a more frequent place of invasion than generally supposed.

[1] Such investigations on a rather large scale are being pursued by a Norwegian, Dr. Hans Thue; they are as yet unfinished and unpublished, but have given positive results in a large number of cases.

It is surprising how rarely positive results were obtained from the bronchial, hilus, and tracheal nodes, in which otherwise tuberculous changes most frequently and most easily have been found. There were only three positive results, one from these nodes only (in a child 52 days old), one together with the cervical nodes, and one with the cervical and mesenteric nodes. Negative results were obtained from these nodes in several cases in which inoculations from other nodes, especially the cervical, gave positive result. In the 73 cases free from tuberculous infection, microscopic examination of these nodes was made in 27 cases and inoculations in guinea pigs in 16 cases. One reason why these nodes were less thoroughly examined, especially less than the cervical nodes, is the fact that they are more rarely enlarged in little children. However, as general experience as well as some of the researches on latent tubercle bacilli previously mentioned point to the frequency of tuberculous infection in these nodes these investigations also ought to be continued on a larger scale.

The cases of simultaneous occurrence of latent tubercle bacilli in several or even all groups of lymph nodes are of interest. We shall return to these cases when discussing the localization and points of invasion of tuberculosis, as they ought to be discussed in connection with cases in which tuberculous lesions simultaneously exist in several groups of lymph nodes.

As already mentioned on several occasions, the swelling of the different groups occurs at different times so that most of the groups are found enlarged when the children have grown older. My material must be considered quite well suited to aid in forming an opinion on on this point as it chiefly consists of children dead within the first year or even a few months after birth. It is a noteworthy fact that the cervical and (perhaps somewhat later) the mesenteric nodes first become swollen. This is the general rule. In a given case the cause of death naturally is of great importance. Of the cervical nodes the *nodi cervicales profundi superiores* show a particularly early enlargement (these nodes drain the pharynx, larynx, tongue, etc.). The bronchial, hilus, and tracheal nodes, on the other hand, are involved later. In the

first weeks or months after birth these nodes are not swollen and so small as to be difficult of recognition. Hence, the irritating substances, including the micro-organisms, which cause the swelling of the nodes, appear to reach the nodes in the chest relatively late. This is clearly borne out by the study of cases.

As a result of these investigations we have the demonstration in a comparatively large number of cases, of the presence of latent tubercle bacilli in the lymph nodes, and especially in the cervical nodes. The following questions then arise: *Do these bacilli possess their usual virulence? How long may the bacilli be supposed to have lain latent in the lymph nodes?*

Both questions are extremely difficult to answer. With reference to the first question, it might seem probable that bacilli which are found in lymph nodes and may be supposed to have been there for some time, should be possessed of comparatively little virulence, having produced neither demonstrable changes nor a further infection of the organism.

Contrary to the conception of former times, it may now be considered settled that tubercle bacilli found in the human body as the cause of various tuberculous affections also possess a variable virulence.

Among other reasons, this is also suggested by the various ways in which tuberculosis may appear and develop. Experiments with different strains of tubercle bacilli and their virulence in animals also seem to point in the same direction. Numerous inoculations in animals of tuberculous material of various kinds have also taught me that the time which elapses before the death of the animals from tuberculous infection varies greatly, a phenomenon not otherwise readily explained than by difference in virulence.

Some knowledge of the behavior of the latent bacilli in this respect might perhaps be gained by studying the results of animal inoculations with special reference to the development of tuberculosis in the animals. It would then soon be noticed that the results were not uniform. It is true that most of them died after two months, or were killed at this time, because they gave signs of advanced tuberculosis. But it was not unusual for the

animals not to die until after three or four months, or it was found convenient to kill them at this time because not until then was the existence of the disease definitely established.[1] And sometimes the disease was comparatively very little advanced even when the animal was killed after three or four months. It even happened that some animals remained healthy while others inoculated from the same nodes became tuberculous and died. Such occurrences cannot well be explained except in two ways—either by assuming that the animals have received very few bacilli, which does not appear probable to me, or that the inoculated bacilli, perhaps few in number, were of comparatively slight virulence. To look for the explanation in a variable susceptibility on the part of the guinea pigs seems less reasonable to me; at least little is known about it.

Everything considered, it appears plausible to assume that the latent tubercle bacilli not rarely have shown a less virulence than usual. This also is in accord with the experiments of Perez and of Manfredi and Frisco.

But *how long* may it now be supposed *that bacilli may lie latent in the lymph nodes* or elsewhere in the body? This is a question of the greatest importance, especially so far as the different theories concerning modes of infection in tuberculosis are concerned. The idea of the prolonged latency of tubercle bacilli in the organism is well known. V. Baumgarten, in particular, has always brought it forward when advocating the frequency of intrauterine infection, and believed that the explanation of cases of tuberculosis appearing late in childhood or in adults must be sought in a latency extending over even long periods. And v. Behring, as is well known, has recently advocated the same idea; but he placed the infection in early childhood; then, as it appears from his writings, the bacilli should remain latent in order later, perhaps first in adult life, on some occasion to break out and cause damage. As to a period of latency reaching back to intrauterine life, we shall come back to it in a subsequent chapter. At this time suffice it to remark that there is not

[1] The lesions always appeared in this order: swelling of the inguinal nodes on the right side; then of the retroperitoneal nodes, spleen, and liver; later of the tracheal, bronchial, and cervical nodes, and lungs.

much evidence on which to consider congenitally latent tubercle bacilli as frequent or of practical importance (as is true of congenital tuberculosis in general). Still, in this connection I will also express the opinion that, while I must take issue with v. Baumgarten as to his hypothesis in general, I believe that congenital infection is more frequent than commonly believed, which is also true of latent tubercle bacilli in the lymph nodes.[1] Yet I must assume that most tuberculous infections occur after birth. This, however, does not bring us nearer to a solution of the question of the duration of latency. It is extremely difficult to express anything definite concerning this. The reduced virulence of the bacilli which I have just emphasized might seem to speak for a prolonged latency, if infection in these cases is not due just to bacilli of slight virulence. As is known, animal experiments seem to indicate that the prolonged sojourn of the tubercle bacilli in an animal organism brings about a reduced virulence (Perez, Manfredi, and Frisco).

On the other hand the age of the children appears to point to a brief stay in the organism. We have seen that latent tubercle bacilli most frequently have been demonstrated in the first two or three years, and especially in the first year. If now the microbes have invaded the body after birth, it must be concluded that they have remained latent a relatively short time, some months (at most a couple of years). This also agrees well with the conclusions reached by Perez and Manfredi and Frisco, as they found that tubercle bacilli injected into animals might remain latent (but enfeebled) for several months (three or four).

Against prolonged latency speaks also the fact that latent bacilli comparatively seldom were demonstrated in older children (over three years), in whom one would expect to find them frequently in case they may remain latent for years. Still, it must be borne in mind that the bulk of the children examined belonged in the first two years. Nor does there seem to be any relation between the degree of virulence of the bacilli demonstrated

[1] In only one of the 18 cases is it directly stated that the mother had tuberculosis; so here the possibility of prenatal infection was present.

(judging from the results of inoculations in animals) and the age of the child; bacilli of ordinary or high virulence were found in children over two years in whom bacilli of low virulence should have been expected, and conversely, tubercle bacilli of low virulence were found, particularly in children a few months old.

It is thus seen that my investigations do not support the view that virulent tubercle bacilli may remain latent for years in the body, and particularly in the lymph nodes. Probably this cannot be proven. From what has been stated, at most the conclusion may be drawn that a latency of several months seems likely. I believe, however, that at present a latency of several years cannot be denied, though it is not probable, as little evidence now can be brought in favor of such a view.

It is also the general opinion that a latency of years is neither proven nor probable. This opinion has, among others, been strongly maintained by Cornet. Lubarsch,[1] who otherwise does not entirely reject v. Baumgarten's theory, comes to the conclusion that the assumption of prolonged latency (for years) of tubercle bacilli in non-tuberculous foci, without multiplication of the germs or production of pathological processes, is unproven and in itself little probable.

The results of the numerous microscopic examinations and inoculations of lymph nodes from various regions should also be correlated with clinical observations on the frequency of enlargement of the lymph nodes in children and opinions formed as to its relation to tuberculous infection. In this way the nature and frequency of scrofula again become involved, now a burning question. While most authorities consider scrofula, at least in its most common forms, as identical with tuberculosis, others enlarge the conception of the term scrofula to include almost any form of enlargement of lymph nodes, even if other clinical features of scrofula are lacking. The latter view has been most strongly expressed in Cornet's work on scrofula (1900), where two forms are established, one dependent on infection with tubercle bacilli, another mainly on infections of different nature, particularly with pyogenic organisms. This is not the place to

[1] *Loc. cit.*

take up this question in its entirety.[1] I will call attention only to the most important articles in which attempts have been made to determine clinically the frequency of tuberculosis of lymph nodes in children. In these it is partly taken for granted that swollen lymph nodes mean tuberculous infection, although the authors concerned have not had the opportunity to establish the real existence of the latter, and on this basis conclusions, in part far reaching, concerning the freqency of tuberculosis in children, the avenues of infection, as well at the further infection of the organism with tubercle, are reached. Still these contributions are of great importance.

One of the earliest investigators of the frequency of enlargement of lymph nodes in children is Volland,[2] who also deserves credit for having at an early time brought up for discussion the question of the connection between tuberculous lymph nodes in childhood and a later pulmonary tuberculosis. Volland examined 2,506 persons between the ages of seven and 24 years. Of

628	aged	7– 9	years,	607	had	enlarged	cervical	nodes.	96.6 per cent.
724	"	10–12	"	664	"	"	"		91.6 "
722	"	13–15	"	607	"	"	"		84 "
337	"	16-18	"	233	"	"	"		69.7 "
98	"	19–24	"	67	"	"	"		68.3 "

Hence, about 94 per cent of the children between seven and twelve years had enlarged cervical nodes. Volland, however, hesitates to consider all these nodes tuberculous, yet he believes that such infection exists in numerous cases, and on this he bases his theory of infection with tubercle bacilli from skin and mucous membranes by means of dirt and uncleanliness, and here he places the cause of eventual later infection of the internal organs, particularly the lungs.

Neuman,[3] in his review on tuberculosis of the bronchial nodes, also touches on the same question. In 4,883 children from one to nine years old he found a marked chronic swelling (presumably tuberculous) in 309, *i. e.*, 6.38 per cent, and in 2.9 per cent other undoubtedly tuberculous affections. He found most of the cases in the first two years.

Investigations similar to those of Volland have been made by Laser,[4] likewise in school children. He examined 1,216 children, 1,079 of whom had enlarged cervical nodes; at different ages they were found in from 70 to 100 per cent of the cases. Exclusive of other causes of such enlargement (angina, eczema, etc.), he came to the result that in 32.4–58.9 per cent of the cases

[1] Reviews of most recent work of interest on this subject are found in LUBARSCH-OSTERTAG'S *Ergebnisse d. allg. Path. u. path. Anat.*, II, VI, and especially VIII, Abth., 2 (1902).

[2] *Ztschr. f. klin. Med.*, 1893, 23, p. 50; also *Münch. med. Wchnschr.* 1904, 51, p. 87.

[3] *Deutsche med. Wchnschr.*, 1893, 19, p. 202.

[4] *Deutsche med. Wchnschr.*, 1896, 22, p. 500.

tuberculous nodes were present. However, he considers the latter figure rather high as the other etiologic factors are frequently involved. Laser also seeks the source of the infection in inhalation of dust, infection through dirty hands, etc.

In Norway Randers[1] has advocated similar views, emphasizing from clinical experience the frequency of tuberculosis in childhood. In 1899-1901 in the Private Policlinic for Children in Christiania he treated 1,671 new patients; of these 311 were found to be tuberculous, 137 boys and 174 girls. Aside from swollen lymph nodes presumably tuberculous changes in the lungs were found in 99 cases. Most frequently the cervical nodes were affected, regularly also when the axillary, inguinal, and iliac nodes were involved. Tuberculosis of the mesenteric nodes was recorded in 17 cases. Randus also examined 200 boys and about 180 girls in a public school; six boys and nine girls had symptoms of tuberculosis of the respiratory organs, and 182 boys and 160 girls had more or less extensive latent lympathic tuberculosis.

From these investigations it may be concluded that swelling of the cervical nodes is very frequent, and that many clinical data are in favor of the tuberculous nature of this swelling. This result is in full accord with my demonstration of latent tubercle bacilli which were found particularly frequently in the cervical nodes. It may then be considered reasonably certain that lymphatic enlargement, especially cervical, in a large number of cases is due to tuberculous infection, but also, that, in a still larger number of cases it appears to be due to other forms of irritation than tubercle bacilli. And there is also no reason why the tubercle bacilli when demonstrated, might not, at least in part, have been something accidental, in other words, that an enlargement of the lymph nodes previously had existed to which the tuberculous infection had been added.

TUBERCULOSIS IN EARLY CHILDHOOD. CONGENITAL TUBERCULOSIS.

In every study of tuberculosis in children where the probable modes of infection are to be discussed the possibility of the disease being congenital must be taken under consideration. Even if at present only few ascribe much practical importance to this mode of infection, there are, however, prominent pathologists (for instance Baumgarten and his pupils) who still believe in the congenital origin of most cases; and many others, for

[1] *Norsk Mag. f. Laegev.*, 1902, 63, p. 221.

instance Warthin, believe that this mode of infection is of greater importance than commonly supposed.

It is not within the scope of this work to consider this question in its entire breadth; this would also be entirely superfluous as "congenital tuberculosis" has been exhaustively treated in recent years both in monographs and in shorter articles.[1]

I shall only discuss certain phases of this question which come up in connection with my material.

First two cases from the pathological institute of Christiania will be related in which the tuberculosis in all probability was congenital. Ths first case has previously been briefly reported by the late Professor H. Heiberg,[2] the other case I have myself examined.

Case 1 (Professor H. Heiberg's case. Autopsy No. 72, 1874). The child was born at full term (weight 2.5 kg.) and died nine days later. The mother was 33 years old and had had syphilis six years previously; it is not stated whether she also had tuberculosis. The pleura over the left lung was covered with numerous small hyalin tubercles. In the lower part of the left upper lobe was a gelatinous, infiltrated portion of the size of a hazelnut from which purulent fluid could be expressed and in which tubercles were seen. In the lower lobe there was also a pneumonic area of considerable size with numerous tubercles. The right lung presented similar, more advanced changes. There were numerous tubercles both in the mucosa and serosa of the intestines.

Although there are no histological and bacteriological examinations, yet considering the entire postmortem findings together with the definitely expressed opinion of an experienced pathologist of the nature of the lesions, one may assume with certainty that a tuberculous process had been present. Professor Heiberg remarks that it could have been nothing else and adds that "as the process was so far advanced it had probably commenced during intrauterine life."[3]

Case 2 was that of a child, three weeks old, whose father was and still is perfectly well, but the mother had commenced ailing shortly before pregnancy.

[1] Reference may be given to the following: HAUSER, *Deutsche Arch. f. klin. Med.*, 1898, 61, p. 221. CORNET, *Die Tuberculose*, 1899; *Die Scrophulose*, 1900. HILDEBRANDT, *Tuberculose und Scrophulose*, 1902. Review in LUBARSCH-OSTERTAG'S *Ergebnisse d. allg. Path. u. path. Anat.*, 2, 1895; 6, 1899; 8, Abth. 2, 1902. WARTHIN and COWIE, *Jour. of Infect. Dis.*, 1904, 1, p. 140. SCHLÜTER, *Die foetale tuberculöse Infection*, 1902.

[2] *Forh. for det medicinske selskab i Christiania*, 1894, p. 208 (suppl. to *Norsk Mag. for Laegevid*, 1894.)

[3] Unfortunately the organs were not preserved so examination for tubercle bacilli could not be made later.

Early in the course of the latter she developed a dry pleurisy, but later she was quite well and there was then no suspicion of any serious form of tuberculosis. From two to three weeks after delivery, however, signs of extensive pleurisy developed and lasted from two to three months. Afterwards signs of pulmonary tuberculosis appeared, from which disease she died a little over a year after the birth of the child. The child was born at full term, well nourished, and apparently well. The mother nursed it. It showed no symptoms during the first two weeks; then spasms of the glottis appeared, and it died exactly three weeks after birth.

It is to be regretted that the placenta was not examined. The autopsy was made by Professor Peter F. Holst who kindly has placed the material at my disposal.

There was extensive tuberculosis with a large number of tubercles disseminated in various organs, but especially in the lungs where also large consolidated areas were found. The microscopic specimens from the lungs showed an extensive pneumonia with an alveolar exudate rich in cells and fibrin; the exudate here and there showed signs of beginning necrosis. In addition some indistinct tubercles were seen consisting mainly of epithelioid cells and leucocytes and with caseous centers. Everywhere in the tubercles and in the pneumonic exudate enormous masses of tubercle bacilli were present so the specimens in places were entirely red.

Both the extensive and marked changes and the short duration of the life of the child are in favor of intrauterine infection.[1]

We will now consider a little more closely the occurrence of and deaths from tuberculosis in infancy in connection with the question of infection before or after birth. It is evident that the mere occurrence of death from tuberculosis in the first weeks or months after birth must make one think of the possibility of congenital tuberculosis. At what age to draw the line in this respect is a question. Generally cases with death after six months are disregarded, and as a rule attention is only given in this connection to deaths in the first three (or four) months. This is only true on the supposition that it is assumed that tubercle bacilli when once introduced into the body quite soon become active, and that the possibility is not considered that they may remain alive and virulent (but latent) for a considerable period before commencing to exert an influence on the organism. This latter view is the one held by v. Baumgarten, and also maintained

[1] The presence of tubercle bacilli in the blood and internal organs of newborn children (stillborn, or dead soon after birth) has been reported from the pathological institute of Christiania by DR. JENS BUGGE (*Ziegler's Beiträge*, 1896, 19, p. 433). Similar observations have been made in many other places (see WARTHIN, *loc. cit.*).

by v. Behring in his most recent contributions though (contrary to v. Baumgarten) on the basis of a postnatal infection.[1]

We will not here discuss the arguments for and against this hypothesis (see Latent Tubercle Bacilli in the Lymph Nodes) but proceed on the assumption that such latency in general scarcely takes place, and consider the cases of death from tuberculosis within the first three to four months which I have had opportunity to examine.

Case 1.—(Legal autopsy No. 14, 1898.) Child two months and six days old, supposed to have died from ill-treatment. It was learned that the father had consumption, was unable to work, and stayed at home to take care of the children while the mother went out to work. The mother was perfectly well (and was still so three years after the death of the child). She nursed the child when at home. The child was kept in a box or in a bureau drawer; the room was very dirty. The father was bedridden at times, coughed, and expectorated, supposedly in a tin can on the floor; he often had the child in bed with him. It was also stated that the father would chew pieces of bread and give the child. The child died suddenly. The father died of tuberculosis about one and one-half years later.

Autopsy: Length of body, 58 cm.; weight, 4,830 grams. The tonsils were not enlarged, the cervical nodes slightly so. One node was examined microscopically, and no tubercles found. The bronchial and hilus nodes were considerably enlarged and caseous (contained numerous tubercles). The lungs were studded, partly with scattered greyish yellow granules, partly with tubercles in groups, and contained also larger, firm, caseous, consolidated areas which showed beginning softening; microscopically ordinary tuberculous tissue and masses of tubercle bacilli. Here and there tubercles in the liver and kidneys; none in the mesenteric nodes.

The respiratory apparatus must here be considered primarily affected (and probably first the lymph nodes). That the infection occurred after birth must be taken for granted from what has been stated of the father's consumption, etc.

Case 2.—A female child two and one-half months old, who was well until about a month after birth, when diarrhea with mucous and bloody stools set in. Nothing is stated about tuberculosis in the parents or other relatives; the child had never nursed, and was fed on milk.

Autopsy No. 150, 1900: Length, 56 cm.; weight, 2,580 grams. Numerous miliary tubercles in the lungs, especially the right; in the right upper lobe also an almond-sized caseous consolidated portion. The tubercles between the lobes and beneath the pleura were arranged in bead-like rows proceeding from the hilus of the lung. The bronchial and hilus nodes were enlarged to the size of beans, caseated; perforation into the bronchi could not be demon-

[1] See also WARTHIN's work (*loc. cit.*) where the same possibility is emphasized (point 8 in his conclusions).

strated. The cervical nodes were enlarged; in a few of them as well as in a few mesenteric nodes caseous foci were found. Tubercles were found in the spleen, liver, and some of Peyer's patches.

In this case of advanced tuberculosis the bronchial and hilus nodes seem to have been primarily infected, and from these the lungs, and secondarily the intestine, mesenteric (?) and cervical nodes. There is no information of the existence of tuberculosis in the parents; it is probable that the child was infected after birth; and there is nothing in the distribution of the tuberculous changes to speak against their development after birth.

Case 3.—(Autopsy No. 135, 1900.) Child 10 weeks old, whose mother had died of pulmonary tuberculosis seven weeks after the birth of the child. The mother also had syphilis and the child had congenital syphilis. When six weeks old the child entered the dermatological ward of the hospital; how it previously had been fed is not known. At the autopsy the lungs were found to contain numerous tubercles which in places had coalesced to form large caseous masses; the left lower lobe contained a caseous focus of the size of a hazel nut. The lymph nodes at the hilus were of the size of beans and caseous. There was also a right-sided tuberculous fibrinous pleuritis; tubercles were seen in the spleen and liver. No changes in the intestinal tract. Microscopically typical tubercles were found, and huge masses of tubercle bacilli.

In this case the possibility of intrauterine infection must be admitted, although the most important localizations do not point in that direction. But nothing speaks against an infection after birth, for which abundant opportunity had existed; if so the respiratory tract most likely was the atrium. (However, the cervical nodes, unfortunately, were not thoroughly examined.)

Case 4.—Autopsy of a child not quite two months old (born May 1, died June 30). Weight 2,250 grams. Beneath the pleura of the posterior surface of the lower lobe of the left lung a few tubercles of pin-head size were seen. In this lobe there also was a pea sized nodule filled with a greenish yellow thick material surrounded by a caseous zone and outside this by yellowish-white tubercles. In the right middle lobe was a similar nodule surrounded by small tubercles. The bronchial nodes were enlarged, caseous, and softened in their central portion. Several tubercles in the spleen, and small tuberculous ulcers in the ileum; the mesenteric nodes were considerably enlarged, softened in their central portion.

It was stated that the mother had pulmonary tuberculosis, and died 16 days after the birth of the child. The child was partly nursed by another healthy woman. A rash appeared when it was a couple of weeks old. It died of diarrhea.

Here the possibility of either intrauterine infection or infection from the mother after birth must be admitted. The distribution of the tuberculosis would fit either mode.

Case 5.—Child two months and 26 days old. The mother had pulmonary tuberculosis and kept the child with her more than a month before it was taken to the hospital. The child died of considerably advanced tuberculosis of the lymph nodes of the chest and of the lungs. There is nothing to speak against the assumption—in fact, to a certain degree it seems likely—that the child was infected from the mother after birth and died of this infection before reaching the age of three months.

Case 6.—Child three months and nine days old, who had stayed with its consumptive mother for two and one-half months, hence abundantly exposed to infection. It died of an extensive tuberculosis of the lymph nodes of the chest and abdomen; there were also considerable pulmonary tuberculosis and small tuberculous intestinal ulcers. Probably this child was infected by the mother after birth; at least the lesions found are easily compatible with this view. On the other hand, it is difficult to tell whether the infection took place through the respiratory or digestive tract.

Case 7.—The same reasoning is still more plausible in the case of a child four months old, who had been with its tuberculous mother over three months, and had died from tuberculosis of considerable extent of the thoracic and abdominal organs. Here also infection from the mother after birth, either through the respiratory or digestive tract, seems probable.

Case 8.—Child two months and two days old who was with its tuberculous mother for a month when the mother had to be taken to a hospital, where she died from pulmonary tuberculosis. The child suffered from enteritis, and steadily lost in flesh. At autopsy the bronchial nodes were much enlarged and tuberculous, the mesenteric nodes also enlarged, and there were miliary tubercles in all the organs. Here it cannot be decided whether the child was infected before or after birth; either possibility must be admitted.

One might also in this connection consider the cases in which tubercle bacilli were found in the lymph nodes of little children although these cases are much more uncertain. Thus, latent bacilli were demonstrated in the cervical nodes of children two months, three and one-half months, and four months old, and in the bronchial nodes of a child one month and 22 days old. The mother of the latter child was tuberculous; the infection might have been intrauterine, or more likely postpartum (from the mother) without tuberculous lesions yet having developed. In the case of the other three, and older children, postnatal origin is still more likely; nor were there any statements in these cases that the parents suffered from tuberculosis.

From the foregoing descriptions and remarks it will be seen that Case 1 in all probability must be regarded as an instance of infection from the father after birth.[1] In Case 2 nothing was known of the health of the parents. In the other six cases, on the other hand, the mother was tuberculous and the possibility of intrauterine infection present, but infection might also very well have taken place after birth. It may also be noted that in two cases the children were born with syphilis, a combination which is not rare; at least it appears as if children with inherited syphilis are comparatively prone to tuberculosis.

What does general experience teach as to children born of tuberculous mothers?—First it must be stated that tuberculous women not rarely abort or give birth to still-born infants in which tuberculous changes rarely have been demonstrated. The causes of the abortions and still-births seem to vary much: infection of the fetus in utero in rare cases; intoxication of the fetus from the mother on account of the latter's tuberculosis; poor condition of nutrition in the mother and thereby also of the fetus; and tuberculous changes in the placenta with their effect on the nutrition of the child must not be forgotten. It seems as if the latter changes are demonstrable comparatively often if only sufficiently painstaking examination is made. In this connection reference may be made to Warthin's work and to the recent investigations of Schmorl and Geifel.[2]

In this connection the following observations are of interest:

1) A woman 27 years old who for nine years had had symptoms of pulmonary tuberculosis, two months before death gave birth to an eight month's fetus (the latter unfortunately was not submitted for examination). The autopsy of the woman revealed chronic pulmonary and laryngeal tuberculosis, tuberculous peritonitis, left-sided salpingitis (of long standing) and a tuberculous endometritis; the placental site was uneven and nodular, and the whole inner surface of the uterus covered with yellowish white caseous masses which were especially abundant at the placental site. Microscopically, masses of degenerated tubercles, and tubercle bacilli. Here it is natural to suppose

[1] Infection from the father during conception through the sperm without infection of the mother must be considered so rare—if it occurs at all—as to be left out of consideration.

[2] *Munch. med. Wchnschr.* 1904, 51, p. 1676. They examined placentas from 20 tuberculous women and could demonstrate microscopically tuberculous changes in nine (*i. e.*, 45 per cent), both with advanced and beginning pulmonary tuberculosis. In three of these cases they could not demonstrate tubercles or tubercle bacilli in the fetus (inoculation of guinea pigs was not employed).

that the tuberculous endometritis antedated and brought on the premature delivery; but an infection of the uterus from the tubes after childbirth cannot be excluded.

2) July 5, 1904 a six month's fetus was examined born of a mother with advanced pulmonary tuberculosis of about six months' standing. The child lived five hours after birth, was a little over 30 c.m. long and weighed 620 grams. Nothing worthy of note was found in its internal organs; a guinea pig was inoculated with pieces of liver and spleen; it was killed September 18 and no changes were found. The placenta weighed 180 grams and measured 10x10 c.m.; in its marginal portion several large infarcts were seen; otherwise no change. Two guinea pigs were inoculated July 5 with pieces of placenta; they became emaciated and when killed on September 18 showed signs of advanced tuberculosis proceeding from the point of inoculation. Microscopic examination failed to demonstrate tubercles or tubercle bacilli. The case will be further investigated.

However, it has been shown that most children born dead or alive of tuberculous mothers show no signs of tuberculous infection.

In this connection it is noteworthy that in the last six years 261 infants still-born or dead a few days after birth were examined at the pathological institute. Not a few were born of tuberculous mothers. Tuberculous changes were not demonstrable in a single case.

It must also be mentioned that among children which had lived for some time many were born of tuberculous mothers but were themselves without any trace of tuberculosis. The following cases will serve as examples:

1) Autopsy 70, 1902. Child, age 10 months; mother had pulmonary tuberculosis. The child died of bronchopneumonia. The cervical nodes were considerably enlarged, light greyish red in color. Nodes from both sides of the neck were inoculated into two guinea pigs, one of which died 21 days later (of enteritis), the other was killed after four months. Both animals were entirely free from tuberculosis. Both tonsils and three cervical nodes were examined microscopically, with negative result. The mesenteric and bronchial nodes of the child were very slightly enlarged, with no sign of tuberculosis.

2) Autopsy 128, 1902. Boy 11 months old whose mother died of pulmonary tuberculosis when the child was nine months old. It is stated that the mother at times masticated food for the child. The child died of enteritis, rickets, and bronchopneumonia. The cervical lymph nodes were swollen, soft, greyish red; two guinea pigs were inoculated with material from these nodes on July 19; they were killed November 7 and were in every respect normal. The lymph nodes at the root of the lungs were of the size of beans, the mesentric nodes were also enlarged, and pale. Microscopic examination of the various lymph nodes, tonsils, and spleen revealed no sign of tuberculosis.

3) Autopsy 45, 1903. A boy three months and 20 days old whose mother died of pulmonary and laryngeal tuberculosis two days after the birth of the child. The child was much emaciated, with the clinical findings of chronic staphylococcus pyemia. The autopsy revealed pale pea-sized cervical nodes, swollen axillary nodes, mesenteric nodes enlarged to the size of almonds (tracheal and bronchial nodes not enlarged), and enlarged spleen. March 12, two guinea pigs were inoculated with cervical nodes, one with axillary nodes, one with mesenteric nodes, one with spleen, and one with liver tissue; all animals were killed May 7, and no trace of tuberculosis was found in any of them. The cervical and mesenteric nodes, the spleen, and the liver were found normal on microscopic examination, and tubercle bacilli were not found in them.

4) Autopsy held November 7, 1903, on a child four weeks old, born seven weeks before full term. The mother had pulmonary and laryngeal tuberculosis and died 13 days after the birth of the child (father healthy). The child was bottle-fed, and brought to the hospital after the mother's death suffering from enteritis from which it died. The cervical and mesenteric nodes were slightly swollen, the tracheal nodes not enlarged. On November 7, four guinea pigs were inoculated with cervical nodes, mesenteric nodes, liver, and spleen respectively; all were killed December 22 and no tuberculosis detected. Microscopic examination of the tonsils and a group of mesenteric nodes gave negative results.

5) Autopsy 37, 1904. Child two months and five days old, born 10 weeks prematurely of a tuberculous mother. It was brought to the hospital soon after birth and died from marasmus and bronchopneumonia. The cervical and mesenteric nodes were enlarged, soft, light red. Two guinea pigs were inoculated March 5 with cervical and mesenteric nodes; they were killed May 3 and found to be perfectly healthy. Ten mesenteric nodes, eight cervical nodes, liver, spleen, and kidneys were examined microscopically with entirely negative result.[1]

The following observations may also be included here; the last one is also of medicolegal interest.

6) April 26, 1904, I received a six months' fetus born of a tuberculous mother (whose pulmonary tuberculosis had mainly developed in the last seven months). The placenta was not received. The autopsy of the fetus presented nothing of special interest; there was no sign of tuberculosis. One guinea pig was inoculated with pieces of spleen and mesenteric nodes, another with liver; both were killed two months later and found healthy. Microscopic examination of liver, spleen, and lungs failed to show tuberculous lesions or tubercle bacilli.

7) A married woman a little over 20 years old was confined to bed with pulmonary tuberculosis for many months. She had not the faintest suspicion of being pregnant. After staying in bed for seven months she suddenly and entirely unexpectedly gave birth to a boy; 10 days later she died from pul-

[1] These observations are in accord with those made at other pathological institutes; for instance, see report of LUBARSCH (*Arbeiten aus der path.-anat. Abtheilung des Hygienisches Instituts zu Posen*, 1901, pp. 7-17.

monary tuberculosis. The child was extremely emaciated, weighed 2,400 grams. It remained well for two years when it became sick first with gastro-enteritis, then cough, and died two years and three months old. The post-mortem showed advanced tuberculosis in the digestive tract, the lungs, and the brain. The possibility of a congenital tuberculous infection may not be excluded.

All these observations like similar ones published elsewhere speak against frequent intrauterine transmission of tubercle bacilli. Whether intrauterine transmission is sufficiently rare to be left out of consideration practically (as claimed by Robert Koch) is another question. With the cases related in mind I must lay somewhat more stress on intrauterine infection than is generally done, and declare myself in accord with Warthin and Cowie[1] in this matter.

Here another question suggests itself: Is it possible from the extent of the tuberculous lesions (in children dead of tuberculosis within the first months) to conclude with any certainty whether the infection took place before or after birth? This leads up to still another question which hitherto has received little attention: Can tubercle bacilli transmitted to the child in utero remain latent in the organs, for instance, the lymph nodes, later to proliferate and cause active tuberculosis (see v. Baumgarten's theory). Warthin and Cowie also touch on this question as they state in their conclusion (8) that "a true latent congenital tuberculosis is both possible and probable." Schmorl and Geipel[2] express themselves as opposed to the assumption of such a prolonged latency. They believe that tubercle bacilli not rarely pass from a tuberculous mother to the fetus; if few in number they soon perish; if more numerous they will produce in the fetus a tuberculosis which will cause death in early childhood.

Material with which to furnish proof in favor of prolonged latency of tubercle bacilli transmitted in utero is still very scanty. Thus it seems probable in cases of successful inoculations from blood or organs of new-born infants without tuberculous lesions that the transmission of tubercle bacilli took place during or shortly before birth. Still, the possibility of prolonged latency of the bacilli after an eventual intrauterine infection is to a

[1] *Loc. cit.* [2] *Loc. cit.*

certain extent supported by the fact previously stated that lymph nodes of children of various age have contained latent tubercle bacilli demonstrable by animal inoculations.[1]

The theory of congenital latency of tubercle bacilli, however, is far from being proved. It seems to be true in general that the body of the new-born is a favorable soil and that infection with tubercle bacilli is rapidly followed by active tuberculous inflammation.

How early may one suppose that a child infected with tubercle bacilli immediately after birth dies of tuberculosis? It is of course out of the question to give definite figures in days, weeks, or months. Many factors are brought into play: The quantity of infective agent, its virulence, and the power of resistance in the body. The point here is to determine the shortest time after birth in which death from tuberculosis can occur when an intrauterine infection may be excluded. Hence we can only use cases in which the mother was healthy. Our Case 7 seems to be one in point, as the mother is still living and healthy, while it seems that the father infected the child after birth. This child died at the age of two months and six days.

In the literature similar cases may be found. Thus Kossel[2] and Wassermann[3] describe a child 10 weeks old which died of tuberculosis. They thought it had been infected between the ninth and 17th day after birth, during which time it was kept in a room in which there was a large quantity of tuberculous sputum. The mother was healthy. Hochsinger[4] describes three cases of fatal tuberculosis in infants. The two infants whose mothers were tuberculous died at the ages of 31 days and 16 weeks. Here the possibility of intrauterine infection was present. The third infant died at the age of 38 days, and the mother is said to have been free from tuberculosis (nothing is said about the father). In this case infection after birth seems most probable.

Haushalter[5] also has described a child two months old with advanced tuberculosis, whose mother was healthy, while the father had tuberculosis. It was thought the child had been infected after birth.

From this experience it appears safe to state that a child infected with tubercle bacilli after birth may die from tuberculosis within two months.

[1] It is of interest to bear in mind that congenital tuberculosis is quite frequent in certain animals, especially calves; on the other hand I have no knowledge of investigations into the occurrence of latent tubercle bacilli in calves.

[2] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1896, 21, p. 59.

[3] *Münch. med. Wchnschr.*, 1894, 41, p. 713.

[4] Cit. by DÜRCK in LUBARSCH-OSTERTAGS *Ergebn.*, 1895, 2, p. 196. [5] Cit. by DÜRCK, *loc. cit.*

Antvord[1] seems to place this age limit too high, when he states that not more than three or four months need elapse between the primary infection and death from tuberculosis. He also maintains that such cases are rare in which infants from six to seven weeks old die from so advanced tuberculosis that intrauterine infection must be assumed.

Cornet,[2] on the other hand, seems to place the limit rather low, when hestates that tuberculosis scarcely occurs in the first three or four weeks, "that is, not until the disease can be explained by a postnatal infection."

From the available facts it seems to me unlikely that a child infected after birth should die of tuberculosis when only from three to four weeks old. (It might be possible if it also had inherited syphilis, which perhaps promotes the development of tuberculosis.) But at any rate one may suppose that a child may die of postnatal tuberculous infection when eight weeks old, and probably even when only five to six weeks old.

THE MAIN LOCALIZATION AND POINTS OF INVASION OF TUBUCULOSIS IN CHILDHOOD.

The primary localizations of tuberculosis is now one of the burning questions, especially since Robert Koch's notable address before the Congress in London in 1901, in which he maintained that man is not infected with bovine tubercle bacilli, which are of another species than the bacilli in man, and stated as proof, that primary infection of the intestinal tract is a great rarity. The proof that this difference in species does not exist may be considered established by the numerous experimental investigations made, especially in Germany, England, Denmark, etc.

Concerning the rarity of primary localization in the intestinal tract considerable material previously existed, but too little attention had been directed to this localization. The older statistics also have been worked out from the one-sided point of view that infection as a rule takes place by inhalation and that the respiratory organs most frequently are primarily attacked. Interest in these questions was aroused by Koch's address, and still more so when v. Behring in 1903 advanced his hypothesis—so diametrically opposed to that of Koch—that infection most frequently

[1] *Norsk Mag. f. Laegev.*, 1895, 55, p. 1013. [2] *Loc. cit.*

takes place through the intestinal tract and already in infancy (but *after* birth as had also been maintained by Koch.)

Before relating my own investigations on this subject it may be of interest to consider the more important contributions to it in the literature. It must at once be noted that these contributions vary greatly in their scope and in their value. Some of them have been written from a clinical point of view, while a larger number are based on autopsy material, as a rule from long periods, most of the autopsies generally having been performed by others than the reviewer of the entire material. Many of these reviews are very one-sided, particularly because often the examinations had been made with the view to demonstrate the largest possible number of primary changes in a certain system of organs (e. g., in the intestinal tract in the English statistics.)

It is a constant feature that the mouth, throat, and their regional lymph nodes scarcely have received attention, except in the statistics of surgeons and pediatricians, where these very localizations dominate completely because they are the parts most readily examined in the living subject. Some statistics are only concerned with deaths from tuberculosis in children; others only with latent tuberculosis as it is found, for example, in children dead of acute diseases, such as diphtheria, etc. (Geill; Heller; Councilman, Mallory, and Pierce, etc). Nor do all these deal with children of the same periods of age. Some only consider children under five years, others under 10 or 12 (especially the English), others under 15 (which is also our limit), and again others simply throw adults and children together. The nationality of the author also seems to play a certain part. The English authors, at least, have results which generally differ greatly from those of the Germans (though the results have been more even in the last couple of years). However, the material has constantly grown larger; it has been treated from more numerous points of view; and hence has become more valuable.

We shall only note some of the more important contributions, especially recent ones and those from the Scandinavian countries.

Froebelius, whose extensive work already has been mentioned, also considers the localizations of tuberculous lesions. He believes the disease most

frequently originates from the bronchial nodes, in some cases from the mesenteric nodes, and that inhalation tuberculosis entirely outranks the alimentary form. He scarcely pays attention to congenital forms, though in 20 of his cases death occurred in the first two months (for instance, one child three days old; one, one week; one, two weeks; three, three and one-half weeks, etc.). In later childhood, however, both tuberculosis of the bronchial nodes and miliary tuberculosis decrease in frequency while that of the intestines and mesenteric nodes increases. Froebelius also points out that pulmonary tuberculosis in infants often appears in the trail of intestinal and pulmonary affections.

Geill, in his extensive work[1] (from Denmark), is mainly concerned with lymphatic tuberculosis. In 288 cases of latent tuberculosis in children the bronchial nodes were involved 262 times; cervical, 39; lungs and pleurae, 125; mesenteric nodes, 59; spleen, 47; and the liver 38 times. In 142 cases the lymph nodes only were attacked, namely the bronchial nodes 109 times; mesenteric, 22 times; bronchial and mesenteric, seven times; bronchial, cervical, and mesenteric, three times; bronchial and cervical, once. In 22 cases the tuberculous process was considered arrested and in 40 cases almost completely so. Of the 288 cases (from 902 autopsies), (1) the mesenteric nodes alone were affected in 23; (2) both the abdominal and thoracic organs in 77 cases; possibly 11 of these cases must be added to the first group as probable primary intestinal infections the number of cases of which then would be 34, or 11.8 per cent of all tuberculous cases. (3) The thoracic organs were affected in 188 cases (in 78 cases the bronchial nodes and lungs together, the former probably primarily), sometimes also the cervical nodes; in 109 cases the bronchial nodes (in one case also the cervical nodes). To this group must also be added 66 cases of the second group as of probable thoracic origin, which gives a total of 254 cases or 88.2 per cent of all tuberculous cases. Of the lymph nodes in the chest the hilus nodes were oftenest attacked; then those at the bifurcation of the trachea; in these groups the changes were marked. When the cervical nodes were involved Geill believed them to have been secondarily infected by an ascending tuberculosis. He concludes that inhalation tuberculosis is the most frequent form in children as well as in adults.

Müller,[2] in 150 cases of fatal tuberculosis found the lungs involved in 139 cases; the lymph nodes in 126; and of the latter the bronchial nodes in 103 cases; the mesenteric nodes in 72, etc. In the 59 latent cases the lymph nodes were involved in 44 cases, (bronchial, 27; cervical, six;[3] mesenteric, six; mediastinal, two etc.), the lungs in 34 cases etc. Müller believes that the intestinal tract, on the whole, is a rare point of invasion, and he points out that the mesenteric nodes are much more rarely primarily attacked than the bronchial. In Hecker's[4] 97 fatal cases the lymph nodes were affected in 90 cases: bronchial and mediastinal, 63; mesenteric, 26; cervical, 12; retroperitoneal, nine; the lungs were involved in 74 cases; the intestines in 22,

[1] *Loc. cit.* [2] *Loc. cit.*

[3] However he believes that this figure is too low as these nodes had not been sufficiently examined.

[4] *Loc. cit.*

etc. In the 50 latent cases the localization was in the bronchial nodes in 38 cases; mesenteric, five; cervical, three; also frequently in the lungs but as a rule secondarily from the bronchial nodes.

Boltz,[1] in his 176 fatal cases of tuberculosis in children, found the respiratory organs attacked in 131 cases; involvement of the bronchial nodes was absent in three only. In 72 cases (41.3 per cent) the digestive organs were affected, how often together with the lungs is not stated.

The result of the study of the frequency of the various primary localizations of tuberculosis by English authors are quite remarkable. Thus Woodhead[2] in 127 carefully examined cases of tuberculosis in children found tuberculous ulcers in the intestines in 43 cases (it is not plainly stated whether the respiratory organs also were affected). The mesenteric nodes were tuberculous in 100 cases; and affected alone in 14 of these (or in 11 per cent of the autopsies, especially at the age between one and five and one-half years; together with the hilus and mediastinal nodes in 69 cases, with the lungs in 62 (most frequently recent tuberculosis); and associated with tuberculous enteritis in 18 cases. In 27 cases (about 21 per cent) the hilus and mediastinal nodes were involved when the mesenteric nodes had escaped.

Still,[3] in his 269 cases of tuberculosis in children found the lungs attacked in 210 cases, the intestines and peritoneum in 141 cases. However, in 46 cases the point of primary invasion was difficult to locate. The lymph nodes give the best starting point to determine this. He came to the conclusion that the lungs were primarily attacked in 138 cases (105 certain, 33 probable), of these seven were under six months; 18, 6–12 months; 38, one to two years; 20, two to three years; 20, three to four years; 12, four to five years; nine, five to six years, etc.; the intestinal tract was primarily involved in 63 cases, or 23.5 per cent (53 certain cases, 10 probable); five of these were 6–12 months old; 15, one to two years; six, two to three years; 11, three to four years, etc. Infection by way of the lungs was most frequent; after the age of five years, however, equally frequent by the intestinal tract. It is also noteworthy that the ears, according to Still's investigations, were the point of invasion in 15 cases or seven per cent (especially in the first two years), the fauces only twice. Of 43 cases of latent tuberculosis the lungs were affected in 26, the intestines in 16 and the ears alone in one case (the mesenteric nodes alone in nine cases.)

Carr's[4] findings in autopsies on 120 tuberculous children agree with those of Still. He found the starting-point to be in the chest in 79 cases, in the abdomen in 20 cases or 16.6 per cent (in six cases a decision was impossible). In 26 cases with little advanced or ancient tuberculosis, the chest alone was attacked in 12, the abdomen alone in seven, the mesenteric nodes alone in five cases. In 53 cases under two years the disease was found to have commenced in the chest 43 times, in the abdomen five times; in 27 over five years 12 times in the chest and six times in the abdomen.

[1] *Loc. cit.*

[2] *Report from the Laboratory of the Royal College of Physicians*, Edinburgh, 1889. Vol. I.

[3] *Brit. Med. Jour.*, Aug. 19, 1899, 2, p. 454.

[4] *Brit. Med. Jour.*, Sept. 2, 1899, 2, pp. 627, 814.

Shennan,[1] collected 355 cases of tuberculosis in children from an Edinburgh hospital. He succeeded in determining the primary focus in 331 cases and 93 of these were cases of alimentary tuberculosis; in a later series of 45 cases, 11 were abdominal; in all 104 abdominal cases in 376, or 27.8 per cent. Carr cites investigations of Guthrie[2] according to which tuberculosis in childhood by far most frequently starts from the chest.

Still, Carr, and Shennan pay little attention to the organs of the neck. On the other hand, Walsham[3] mentions investigations by Batten (from St. Bartholomew Hospital in 1895) according to which in 100 tuberculous children the cervical nodes were attacked in 14 cases; the mesenteric nodes were tuberculous in 63 cases, and in 54 of these the nodes in the chest were also involved. Still and Carr, while giving high figures for the number of cases of abdominal tuberculosis, still maintain that the organs of the chest and the common atrium are most frequently primarily attacked. Raw,[4] however, gives most surprising figures, claiming to have observed 273 cases of tabes mesenterica. In 38 of these he performed autopsies when the lungs often were entirely unaffected (however details are lacking). Conditions are different according to the figures from America given by Hand[5] concerning 115 cases of tuberculosis. The lungs were apparently primarily involved in 75 cases (65.2 per cent), the mesenteric nodes in 10 (8.7 per cent), the tonsils in one case, primary focus not determinable in 29. The bronchial nodes were involved in 94 cases, the lungs in 70, the mesenteric nodes in 53 cases, the intestines in 28 etc. Most of the deaths occurred in early childhood, 60 under two years; 25, two to five years; 30, 5 to 12 years. Hand supposes that most cases are due to air infection, while in some cases infection is through food and by way of the intestinal tract. Moreover, anatomically these cases cannot be separated (as shown by Ravenel's experiment of feeding tuberculous material to monkeys followed by the development of primary tuberculosis of the thoracic organs), or at least with difficulty. This is contrary to Still who directly determined the point of invasion from the group of lymph nodes most affected.

Among other American observers Northrup[6] in 125 cases found the starting point in the alimentary tract three times. Bovaird[7] in 75 cases from a New York infant asylum found the bronchial nodes involved in all. Holt,[8] in 119 autopsies from infant asylums in New York found no case of probable primary gastrointestinal localization (although the mesenteric nodes were involved in 35 per cent of the cases and the intestine in 37 per cent).

Heinrich Schmidt[9] in 336 children under 10 years dead from tuberculosis concluded that the disease was primary in the respiratory tract in 230 (68.5 per cent), in the lymph nodes in 63 cases or 18.7 per cent (bronchial 32, all groups 19, mesenteric six, other groups 12.

[1] Cited by PRICE-JONES (*vide infra*). [2] Cited by PRICE-JONES. [3] *Loc cit.*

[4] *Brit. Med. Jour.*, August 29, 1903, 2, p. 470.

[5] *Proc. Path. Soc. of Philadelphia*, 1903, n. s. 6, p. 132.

[6] *N. Y. Med. Jour.*, 1891, 53, p. 201, cited after PRICE-JONES.

[7] *N. Y. Med. Jour.*, 1899, 70, p. 1, cited after PRICE-JONES.

[8] *Med. News*, 1896, 69, p. 656, cited after PRICE-JONES. [9] *Loc. cit.*

Racynskyi believes that infection in childhood most frequently takes place through the organs of respiration, as he found the bronchial and mediastinal nodes involved in nearly all fatal tuberculous cases, only 17 cases being exempt. He admits, however, that infection may take place by way of the digestive tract.

Monrad[1] also considers the respiratory tract the chief atrium, having found primary localization in the lungs and bronchial nodes in 152 cases and in the digestive tract in only five of his 157 fatal cases.

The figures of Fibiger and C. O. Jensen,[2] however, are different. In 213 autopsies from two Copenhagen hospitals tuberculosis existed as the cause of death, or as a complication, in 116 cases. There were 13 cases of primary affection of the intestinal tract and abdominal lymph nodes and two other cases probably of similar origin, that is, six (or seven) per cent. of all autopsies, or 11 (or 13) per cent of all tuberculous cases; 79 of the autopsies were in children, 25 of whom had tuberculous changes, and in four (or five) cases (16 or 20 per cent) these were primary in the digestive tract. These results, as we see, resemble those of the English observers.

Baginsky's[3] results are different. In his first series of 933 cases there was none of primary intestinal tuberculosis; in a later series of 806 cases, 144 (17 per cent) of which were tuberculous, there were six (4.1 per cent) of primary intestinal tuberculosis (compare the findings of Heller and Councilman whose percentages of tuberculous cases are about the same, but with much greater proportion of the intestinal form).

In Orth's[4] 203 autopsies in children over three months of age there were only two cases of primary intestinal tuberculosis in 47 tuberculous cases, that is one per cent. of all autopsies, and 4.25 per cent of the autopsies in tuberculous cases.

Nebelthau[5] directed his attention particularly to primary infection of the intestinal tract. In 26 autopsies on tuberculous children (from the Halle Polyclinic in three years) he believes primary infection of the digestive tract occurred five times (19.2 per cent), of the respiratory tract nine times (34.6 per cent of the digestive and respiratory tracts 12 times (46.1 per cent). He believes the infection generally could be traced to man.

Ganghofner[6] investigated 973 autopsies in children d ad of acute diseases and found latent tuberculosis in 253 (26 per cent), and primary infection of the intestinal tract in only five of these (one-half per cent of all cases or two per cent of the tuberculous cases).

V. Hansemann[7] among his 8,000 or 10,000 autopsies discovered only 25 cases of primary intestinal tuberculosis; nine of these were in children under 15 years.

In the small but valuable statistics of Councilman, Mallory, and Pierce[8] of 220 children dead of diphtheria with 35 cases of latent tuberculosis (16 per cent) the intestinal tract was primarily infected in 13 cases (5.9 per cent of all cases or 37.1 per cent of the talent tuberculous cases). On the other

[1] *Hosp.-Tid.* 1902, R. 10, p. 300.
[2] *Hosp.-Tid.*, 1902, 4, R. 10, p. 923.
[3] *Loc. cit.*
[4] *Loc. cit.*
[5] *Loc. cit.*
[6] *Arch. f. Kinderheilk.*, cited by HOF and HELLER.
[7] *Berl. klin. Wchnschr.*, 1903, 40, p. 141; 170.
[8] *Loc. cit.*

hand, Morf,[1] who systematically examined the abdominal organs in 232 adult bodies (in 86, or 37 per cent of which there was tuberculosis), found tuberculosis of the abdominal lymph nodes in only two cases where tuberculosis could not be macroscopically demonstrated elsewhere.

Besides the English observers Heller of Kiel and his pupils have thoroughly traced the routes of infection, with special reference to the intestinal tract, and have energetically advocated the frequency of this route. Heller,[2] as the result of a study of the autopsy findings in 714 fatal diphtheria cases in children occurring between the years 1873 and 1894, states that in 140 cases (19.6 per cent) tuberculosis existed as an accidental finding, and in two of these (1.43 per cent) as primary intestinal tuberculosis, in eight cases (5.7 per cent) intestinal and mesenteric, and in 33 cases (23.5 per cent) as tuberculosis of the mesenteric nodes. To these must be added 10 cases (7.1 per cent) with involvement of the mesenteric nodes plus other organs than the lungs, making a total of 53 cases (37.8 per cent) of probable primary intestinal infection, or about one-third of all the latent cases. Heller ascribes the infection to milk from tuberculosis cattle.

Wagner's[3] publication is a continuation of Heller's work. Among the first 600 autopsies held at the Kiel Pathological Institute in 1903, 76 were in children, and in 13 of these (17.1 per cent) there was primary intestinal tuberculosis. He found altogether 28 cases of primary infection through the intestine, namely:

1) Eight cases of tuberculosis of the intestine and mesenteric nodes (all children under 15).

2) Seven cases of primary intestinal tuberculosis with dissemination to other organs (five children).

3) Thirteen other cases where tuberculosis no longer could be demonstrated but where the changes could only be interpreted as due to previous tuberculosis (e. g., calcified mesenteric nodes); three of these were in children, making a total of 16 children of the 76 (21.1 per cent) with primary tuberculosis of the intestinal tract.

Hof[4] has systematically gone through the 15,000 autopsy records of the Kiel institute in the last 30 years to investigate the frequency of primary intestinal tuberculosis. Of 7,683 autopsies in adults tuberculosis was found in 2,697 (35.1 per cent), and of 4,649 in children in 936 (20.1 per cent). In 408 of the latter cases (43.5 per cent) the lungs and intestinal tract were affected, and in 80 of these he considered the intestine to be primarily affected. Adding the cases of undoubted primary intestinal infection we get a total of 235 or 25.1 per cent of all autopsies in children, and primary tuberculosis of the respiratory tract in 527 or 56.2 per cent. Of the 2,697 adult cases 159 (5.9 per cent) were primary in the intestinal tract, while in 84.9 per cent the respiratory tract was primarily involved. Heller, in his most recent article,[5] adds that in 230 later autopsies, 23 of which were in children, he found recent or

[1] *Trans. Chicago Path. Soc.*, 1903, 5, p. 245.

[2] *Deutsche med. Wchnschr.*, 1902, 28, p. 696.

[3] *Münch. Med. Wchnchr.* 1903, 50, p. 2036; 2095.

[4] *Ueber primäre Darmtuberkulose nach 15,000 Sectionen.* Inaugural Dissertation, 1903.

[5] *Berl. klin. Wchnschr.* 1904, 41, p. 517.

old intestinal tuberculosis in 12 per cent of the adults and in 26 per cent of the children.

From the recent statistics of 1,820 autopsies collected by Lubarsch[1] we learn that tuberculous changes were found in 60.6 per cent of all cases, and in 69.1 per cent of those over 16 years of age. In the 297 children tuberculosis was found 63 times; 14 of these cases were instances of primary alimentary tuberculosis 21.2 per cent (or 4.7 per cent of all children). Of 52 children over one year 12 or 23.8 per cent had primary alimentary tuberculosis. Among all the 1,087 cases of tuberculosis there were 56 (5.15 per cent) of the alimentary type. By including cases of coincident infection of the mesenteric and bronchial nodes and of primary tonsillar tuberculosis Lubarsch puts 30.8 per cent as the greatest possible proportion of infection through the digestive tract.

Hof[2] gives the following summary:

Observer	Number of Tuberculous Children	Primary in Digestive Tract		Primary in Respiratory Tract		Both Respiratory and Digestive Tracts Affected	
		Cases	Per Cent.	Cases	Per Cent.	Cases	Per Cent.
Carr	105	20	19.0	79	75.0	6	5.7
Still	247	63	25.5	138	55.9	46	19.0
Kossel	22	1	4.5	13	59.0	8	36.4
Nebelthau	26	5	19.2	9	34.6	12	46.0
Hof	936	235	25.1	527	56.2	103	11.0

Primary tuberculosis of the mesenteric nodes alone was found by Hof in 67 cases or 7.2 per cent; Woodhead in 14 of 127 cases or 11 per cent; Carr in five of 120 or 4.2 per cent; Still in nine of 269 or 3.3 per cent; Bouvaird in three of 200 or 1.5 per cent.

To illustrate the difference in the statistics from different countries Bouvaird gives the following table:

Source	Number of Cases	Primary Intestinal Tuberculosis	
		Cases	Percentage
Germany	236	9	4
France	128	..	..
England	748	136	18
United States	369	5	1

Bouvaird has used most of the statistical data mentioned here but can hardly have included those of Heller and his pupils.

Among the most recent English contributions is that of Symes and Fisher,[3] based on autopsy material from hospitals in Bristol. Among 500 fatal tuberculous cases 102 were in children under 12 years. In 12 of these (11.7 per

[1] *Loc. cit.* [2] *Loc. cit.* [3] *Brit. Med. Jour.* 1904, 1, p. 884.

cent) the abdominal organs were primarily attacked, in 57 (55.8 per cent) the respiratory organs. Of the remaining cases, in four probably the bones and joints were primarily attacked, in four the skin, in one the tonsils, and in four no primary focus was demonstrable. In children under two years the ratio between primary abdominal forms and primary respiratory forms was as five to nine. The following table gives the ratio at various ages:

Age	Ratio
0–12 years	1 : 4.7
10–24 years	1 : 3.9
25–36 years	1 : 9.7
37–48 years	1 : 9.25
49–60 years	No primary abdominal case

Kingsford[1] gives details of 339 children under 14 who died of tuberculosis. One hundred and sixty-two (or 48 per cent) had died in the first two years and 270 (or 80 per cent) in the first five years. Two hundred and twelve (62.5 per cent) were considered infected through the respiratory tract; 64 (18.9 per cent) through the digestive tract; 13 (3.8 per cent) through nasopharynx or middle ear;[2] in 50 cases (14.7 per cent) the primary focus was doubtful. He believes it possible to exclude congenital tuberculosis. He admits, in regard to the first group, that the bronchial nodes, which were most frequently attacked, may be infected from the throat or the intestinal tract. As to the second group, the mesenteric nodes were most frequently affected; infection from food, especially milk, he considers unimportant. Kingsford also has summed up the statistics of various countries as to the frequency of intestinal tuberculosis: English authors (Still, Shennan, Guthrie, Carr, Ashly, Batten) record 214 cases of intestinal tuberculosis among 1,119 tuberculous cases, i. e., 19.1 per cent. If Kingsford's cases are added we have 278 out of 1,458 cases or 19.06 per cent.

American authors (Northrupp, Bouvaird, Holt) found 13 in 434 cases or three per cent. French and German authors nine in 364 or 2.5 per cent.

Price-Jones[3] held 55 autopsies in children and found tuberculosis in 21 cases. He chiefly endeavored to determine whether infection was due to inhaled bacilli or to bacilli swallowed with food, and to decide further, if possible, whether the bacilli came from human or animal sources; he found the latter source to be improbable. Six cases were found to be alimentary; one surely respiratory, and five probably so (including two primarily mastoidal (?); finally nine too extensive to permit of determining the original focus.

In Norwegian literature different opinions on this subject have been expressed.

Professor H. Heiberg,[4] who always devoted much attention to tuberlosis, placed pulmonary tuberculosis first; secondly, intestinal tuberculosis, especially in children; finally, the more local forms among which he gave tuberculosis of lymph nodes a comparatively unimportant place. During the

[1] *Lancet.* Sept. 24, 1904, 2, p. 889.

[2] Kingsford adds that he considers the figures for this group too small.

[3] *Practitioner.* 1903, 71, p. 191.

[4] *Die Tuberkulose in ihrer anatomischen Ausbreitung.* Leipzig, 1882.

lively discussions in 1896-97[1] Bugge and A. Holst advocated the predominating rôle of inhalation tuberculosis, while Malm, with equal energy, insisted on the importance of infection through the digestive tract with secondary localization in the thoracic organs, and Antvord emphasized the important part played by infection in childhood in the cases of tuberculosis which break out in adult life. In 1903-4[2] infection by way of the intestinal tract was again emphasized by K. Thue and Malm. A. Holst[3] demonstrated tubercle bacilli in various "scrofulous" affections, for instance, of the eyes (two cases, of 13 examined) and hypertrophic tonsils (five of six examined). J. Jensen[4] relates a clear-cut instance of probable alimentary tuberculosis. In an otherwise healthy family with nine or ten children one child three years old was taken with ill-defined intestinal symptoms and died of tuberculous meningitis. Some months later, another child, 16 years old, developed diarrhea; then tuberculous arthritis of the elbow; finally pulmonary tuberculosis, and died. They had only one cow whose unboiled milk they all drank; when the cow was killed it was found tuberculous throughout, including the udders.

Let us now turn to the study of my series with a view to determining the primary foci. Of the 39 cases of fatal (or in two cases of rapidly advancing) tuberculosis in Series I we may consider that 19 originated in the lungs and corresponding groups of lymph nodes, five originated in the digestive tract (namely, four in the intestines, generally associated with affection of the mesenteric nodes; one in the tonsils) 15 were of doubtful origin.

The latter 15 cases may be subdivided as follows: Six primary in the respiratory or digestive tract; five in the respiratory tract or osseous system; two were cases of general tuberculosis of lymph nodes; one was primary in skin, boné, or joint; one undetermined.

Of the 33 cases in Series II (1901–4) we may consider that 12 originated in the lungs with their groups of lymph nodes, four in the digestive tract (two in the intestinal tract, one in the cervical nodes, one in intestinal tract or cervical nodes), and 17 doubtful, namely: 13 primary in the respiratory or digestive tracts (seven probably from the intestine, six probably from the cervical nodes); three cases of general lymph node affections; one primary in cervical nodes or a joint.

The difference between the findings of these two series is seen to be that the doubtful cases are most numerous in the second

[1] *Norsk Mag. f. Laegev.*, 1896 and 1897, supplement.

[2] *Norsk Mag. f. Laegev.*, 1903 and 1904, supplement.

[3] *Klinisk Aarbog*, II. 1885, p. 193. [4] *Tidsskrift for den norske Laegeforening*, 1898.

series, in which the material had been most thoroughly worked up, and where infection by way of the throat seems to play a considerable part.

If we combine the two series we have 72 fatal cases (more accurately 69 fatal and three far advanced), in which the primary seat of the disease was located as follows:

Respiratory organs	31
Digestive organs	9
In 32 cases doubtful or in other organs, namely:	
Respiratory or digestive organs (eventually intestine, 13, cervical nodes six)	19
General lymph node tuberculosis	5
Respiratory or osseous systems	5
Throat or joint	1
Bone, joint, or skin	1
Doubtful (partial autopsy)	1

We must also add the 27 cases of latent tuberculosis, most frequently found in the lymph nodes, in which the disease was located as follows:

Intrathoracic lymph nodes only (sometimes also lungs)		16
Cervical nodes, Mesenteric nodes,	*i. e.*, digestive tract 2	1 1
Cervical and intrathoracic nodes		3
Abdominal and intrathoracic nodes		1
General lymph node affection		5

It is also of great importance to include the 18 cases in which latent bacilli were demonstrated, namely in

Cervical nodes only, Mesenteric nodes only, Cervical and mesenteric nodes,	*i.e.*, 15 in digestive tract only	13 1 1
Intrathoracic nodes only		1
Cervical and tracheal nodes		1
All three large groups		1

The latter table alters materially the combined result. If we combine the fatal and all latent cases, $72 + 27 + 18 = 117$ cases, the distribution as to primary seat is as follows:

		Cases	Percentage
Primary in respiratory tract	(31+16+ 1)	48	41
Primary in digestive tract	(9+ 2+15)	26	22
Primary in respiratory or digestive tract	(19+ 4+ 1)	24	20.5
General lymph node tuberculosis	(5+ 5+ 1)	11	9.4
Doubtful, or other primary seats		8	6.8

In connection with these statistics it must first be noted that by primary seat in the respiratory tract usually is meant tuberculosis affecting the lungs or lymph nodes within the thorax (bronchial, hilus, and tracheal nodes). Under primary seat in the digestive tract is included not only tuberculosis of the intestinal tract and the lymph nodes connected with it but also primary tuberculosis of the tonsils and cervical nodes. While the former group of organs as a rule is thought to be infected by inhalation, the cause of primary tuberculosis of the digestive tract is first of all looked for in contaminated food, and hence it seems correct to include the oral cavity, especially the tonsils and the most important lymph nodes in the upper part of the neck.

In connection with tuberculosis of the latter organs (as also of the intestines) the question may always properly be asked whether in at least some of these cases the infection is not due to inhaled bacilli which have become mixed with the food. A separation in this respect, however, is impossible; but it does not seem likely that such a mode of infection should be frequent.[1]

By inoculation of calves to test the virulence of the tubercle bacilli facts might be gained which would aid in deciding in a given case of primary tuberculosis of the digestive tract whether the infection came from man or animals. But such investigations have not been made, and I have been compelled to pass this question by. However, I will here call attention to the fact to which I will return later, that in numerous cases of tuberculosis in children an existing tuberculosis among the surroundings, mainly in the parents, appears to be the most plausible source of infection.

We must critically consider more in detail the most important localizations of tuberculosis in children. We will commence with the respiratory organs. As seen from my tables of 117 cases, probably in over half of these the disease must be looked upon as primary in the respiratory tract (just how many of the 24 cases in group 3 to add to group 2 cannot be stated). And by comparing the other statistical data mentioned we find that the percentage of

[1] I quite agree with what Lubarsch in his last work (*loc. cit.*) states in regard to this question.

primary respiratory infections is steadily declining while that of digestive infections becomes relatively higher in recent statistics (percentages of respiratory infections are: Geill 88.2, Still 51.3, Carr 74, Hand 65, Schmidt 68.5, Symes and Fischer 55.8, Kingsford 62.5).

In this primary respiratory group we include infections of all groups of lymph nodes within the thorax. And the general rule in cases of children is that the lymph nodes are primarily attacked and that the lungs are infected from them. General experience teaches that isolated tuberculosis of bronchial nodes is quite common, while isolated pulmonary tuberculosis with or without a slight and plainly secondary lymph node tuberculosis is a rarity in children; such cases are oftenest met with in late childhood when pulmonary tuberculosis begins to present the features common in adults. As to the nodes in the chest, the common supposition, which also corresponds with the prevalent ideas regarding inhalation, that the bronchial nodes in a narrow sense are those first and most severely affected is not correct. On the contrary, one finds more frequently that the disease is in the hilus nodes, or in the nodes located along the trachea and about the bifurcation, which alone may be affected, or at least most affected. So the impression is created that the bronchial nodes proper are secondarily infected from them. Most frequently caseous foci are found in these nodes; comparatively rarely has microscopic examination revealed latent tuberculosis, or inoculations; latent bacilli. The latter fact is striking compared to the frequency of bacilli in the cervical nodes. It is partly, but not at all entirely, explained by the most extensive examination made of the cervical nodes. It appears that the cervical nodes are more important foci for the deposition of latent bacilli.

We will not at present enter into the way in which these nodes are infected. It lies most closely at hand to assume an air infection; but a descending infection from the cervical nodes or an ascending one from the abdominal nodes cannot be excluded. The predilection of the infection for the tracheal and hilus nodes might point in this direction.

The lungs, then, are regularly secondarily infected. As my

observations plainly show, this most frequently takes place in this manner: that the bronchial nodes rupture into a larger bronchus, generally near the hilus, and thus a secondary caseous bronchopneumonia is set up in the area of distribution of this bronchus. This is a very frequent occurrence (observed 14 times in our cases), and the secondary pulmonary affection is then found in the various lobes, as it appears, without predilection for any particular lobe, though a prevalent localization in the lower lobe is maintained by some. By subsequent breaking down of the caseous portions cavities arise, which are not at all rare in children (observed seven times in our last series). Sometimes cavities are partly due to compression of a bronchus with peripherally located bronchiectases. Nor is even fatal hemoptysis rare.

Such a mode of distribution will regularly lead to the development of progressive pulmonary tuberculosis, and further, often to a dissemination of the disease in the other internal organs where miliary tubercles, as a rule, are found, as in other cases of advanced tuberculosis of some internal organ. The easy and rapid dissemination of tuberculosis through lymph and blood channels is characteristic of tuberculosis in childhood.

However, the lungs may be infected from the nodes in other ways, such as by retrograde transport through the lymph channels. This lymphogenic infection is also quite frequent, though hardly as frequent as the other manner described. The invasion here takes place from the hilus and proceeds along the lymph channels and nodes which accompany the bronchi; the interalveolar connective tissue becomes involved, then an intraalveolar process is set up and finally we have a pulmonary tuberculosis with marked caseation and rapid extension.

Infection of lung tissue from lymph nodes in the chest or elsewhere may also take place by the blood stream; however, according to our present knowledge this route of infection does not appear to be as important as the other routes. We shall not at present enter into the possibility of infection from the intestinal tract after the intestinal mucosa has been passed and tubercle bacilli have entered the blood either directly or after having forced their way through a greater or smaller part of the lymph

vascular system. The occurrence of latent bacilli in mesenteric lymph nodes might point in this direction, and experiments on animals (rabbits, monkeys, etc.) in which, after feeding tuberculous material, only pulmonary tuberculosis was found, have established that this mode of infection is not of little importance. In our cases we most frequently found the lymph nodes of the chest affected together with the lungs, so it is most natural to look for the infection there.

Finally, we see that tuberculous processes, for instance in the lymph nodes, may extend to the lung tissue and infect it directly; however, this is of rare occurrence.

Compared with these secondary infections of the lung tissue from the lymph nodes a primary infection of the former is relatively rare, and as a rule only seen in older children. At the same time we then generally notice a change in the character of the disease, which tends to a more chronic course, to fibrous induration, and to apical localization. It is also in later childhood, after the seventh or 10th year, that the latent and obsolete cases are most commonly met.

In general, the older the tuberculous child, the less prominent the lymph node affections, and the greater the resemblance to the customary adult features as to localization, course, and dissemination. All transitions may occur. On the other hand, in young adults we may encounter features suggestive of pulmonary tuberculosis as seen in children, such as rupture of lymph nodes into bronchi, circumscribed caseous bronchopneumonias, etc. It must be added that with the cases of primary tuberculosis of the respiratory organs we also have included a few cases in which there also was some involvement of the digestive tract (tonsils, cervical nodes, intestines, or mesenteric nodes) but where this involvement was slight and plainly secondary in nature.

We will next consider cases of primary tuberculosis of the digestive tract which, it will be remembered, included infections through the throat as well as through the intestine, and which in our series numbered 26 cases, or 22 per cent. There were nine fatal cases of this class, in six of which the infection was primary in the intestine, while in three we must assume a simultaneous

infection of the intestine and throat. It is quite often necessary to assume primary infection in different localities at the same or different times, as has also recently been maintained by Ribbert and Lubarsch.[1]

In a few of these cases there was so extensive affection of the lymph nodes (also in the thorax) that one might consider other sources of infection of these nodes than the intestine; but the intestine, at any rate, must be considered primarily attacked, as the numerous extensive ulcers could in no manner be accounted for by the tuberculous nodes.

In some of these cases there were also small tuberculous foci in the lungs, but plainly of comparatively recent date, without softening (in one case only demonstrated microscopically), and they must be considered of secondary, perhaps hematogenous, origin; at any rate, they could not account for the infection of the intestinal tract. I, therefore, venture to maintain that in these cases there was a simultaneous infection of two or more parts of the digestive tract (intestine and throat). A few instances will be briefly stated; otherwise the reader is referred to the detailed publication, previously mentioned, where the whole casuistry is related.

1) Girl, 13½ years old, died of suppurative meningitis. Autopsy: Both tonsils and the cervical nodes enlarged, contain numerous tubercles. In the ileum and mesenteric nodes also groups of tubercles. The bronchial nodes were scarcely swollen. Miliary tubercles in the various internal organs.

2) Boy, 13½ months old, whose mother died of pulmonary tuberculosis when he was five or six months old. At the same time he developed a rash and swollen cervical nodes, especially on the right side, diminishing in size downward. The child gradually failed, and died of bronchopneumonia and diarrhea. Autopsy: Cervical nodes on the right side enlarged to the size of a pigeon's egg, caseous, in a continuous chain downward along the neck and into the posterior mediastinum; at the bifurcation and at the pulmonary

[1] Instances of separate infection of different groups of lymph nodes have often been observed, especially: 1) calcareous bronchial nodes and microscopic tubercles in the cervical nodes, and 2) caseous foci in the bronchial and hilus nodes, and in the mesenteric nodes. To relate a few instances: (*a*) In a seven-year-old child, dead of enteritis, there were calcified tracheal nodes and fresh tubercles, demonstrable microscopically, in a cervical node. (*b*) Child, 14 months old, which died of miliary tuberculosis; there were large caseous tracheal and hilus nodes, a few microscopic tubercles in one tonsil, and tuberculosis of a few cervical nodes; finally, numerous tubercles of microscopic size in the mesenteric and retroperitoneal nodes. Here it seems reasonable to suppose that the tonsils and cervical nodes, and perhaps the abdominal nodes, have been infected separately, and later than the nodes in the chest. But extension of the disease from the thorax to the other regions cannot be absolutely excluded.

hila the nodes again were increased in size, caseous, and continued outward along the bronchi. Tonsils normal. No pulmonary tuberculosis, but there were tuberculous ulcers in the intestines and numerous large caseous mesenteric and retroperitoneal nodes.

The clinical and post mortem findings are in favor of a primary infection of the digestive tract, both through the mucosa of the mouth and the intestine, and a descending lymphatic tuberculosis from the neck, and an ascending one from the intestine.

Can we now in these cases obtain data to prove how the infection took place whether by food, and then particularly by bacilli in milk of tuberculous cows, as maintained by Heller; or from human sources, by bacilli which in some way have gained access to the digestive tract, for instance, by contamination of food, or by first being inhaled and then swallowed? Many writers, as Volland, ascribe tuberculosis in children to uncleanliness, the bacilli reaching the oral cavity by means of soiled fingers (on which tubercle bacilli have been demonstrated).

I cannot go farther into this question, which has not been given detailed study. Thus I have not determined the virulence of the tubercle bacilli in the particular cases, as, for instance, might have been done by inoculations in calves (see the investigations of Fibiger and C. O. Jensen). I shall confine myself to pointing to the existence of tuberculosis in the parents or other near relatives in several of these cases, thus rendering an infection from human sources most probable. On perusal of the records in a series of tuberculous children it is, on the whole, striking how often the disease in little children must be brought in relation with disease among the surroundings, especially in the mother.

To the primary infections of the digestive tract we must further add two cases of latent tuberculosis of the cervical nodes and in the mesentery (due to double infection, occurring simultaneously or at different times), and also the 15 cases in which inoculation of guinea pigs revealed latent tubercle bacilli in lymph nodes (cervical, 13 times; mesenteric, once; both, once).

The importance of the latter findings has already been emphasized. Future control investigations are, of course, necessary; yet it may be stated that these findings strongly point toward the frequency of infection with tubercle bacilli through mouth

and pharynx, which also completely agrees with clinical experience regarding tuberculosis of the cervical nodes in children.

At present only hypothetical statements can be made as to whether this finding must be given a more far-reaching importance in the explanation of the origin of tuberculous infection of the internal organs in general—for instance, of the lungs. As these bacilli must have penetrated the mucous membrane of the throat somewhere, it may readily be conceived that they may extend farther along the lymphatics, or enter the blood and subsequently infect the different viscera. The same line of reasoning would hold for the latent bacilli which occur in other nodes, as the mesenteric.

It is peculiar how relatively rarely latent tuberculosis or latent tubercle bacilli have been demonstrated in the mesenteric nodes. Particularly when we bear in mind the observation of Heller and the English authors. This may partly be due to the relatively greater attention given to the cervical nodes. But sufficient microscopic examinations and inoculations of mesenteric nodes were made to incline me, at least at present, to ascribe less importance, so far as frequency is concerned, to infection through the intestinal mucosa than to that through the throat, providing we may draw conclusions as to the point of infection from the localization of the tuberculous process or of the latent bacilli. The figure of 22 per cent as representing primary infection through the intestinal tract is not as high as the figures reached by several recent statistics, but quite high when we bear in mind that the percentage of certain primary infection through the respiratory tract could not be placed at more than 41 per cent. In other words: Of the cases where the the primary localization can be determined with fair certainty, it is found to be in the respiratory tract twice as often as in the digestive tract, according to our statistics. It must, however, be remembered that in the 22 per cent we have included cases of infection of the tonsils and cervical nodes. (Compare Kingsford 3.8 per cent and Batten's 14 per cent of the latter class of cases). If only primary tuberculosis of the intestinal and mesenteric nodes had been included the percentage would have been much less. Our figure

is not suitable for comparison with other statistics of primary tuberculosis of the digestive tract as in most of these attention has only been given to the intestine and mesenteric nodes.

Only Lubarsch also included the tonsils (and also simultaneous infection of other organs) to reach his highest percentage of 30.8.

It is, on the whole, striking how little consideration has been given to infection through the throat and cervical nodes, even by those writers on tuberculosis in childhood who seem to emphasize infection through the alimentary tract. Statements are seldom made concerning it (as by Batten, Still, and Geill who, however, state that the nodes generally are secondarily attacked.) The reason seems very largely to lie in the fact that the organs of the neck and mouth and the upper cervical nodes are not sufficiently examined at autopsies, as well as in the scarcity of microscopic examination and inoculations of material from these nodes. The tonsils (including the pharyngeal tonsils) are an exception to this rule, as within recent years they have been the object of many systematic investigations. The percentages of infection (four to five) are not high, but if these cases were included and also the cervical nodes examined, I have no doubt, bearing my own observations in mind, that this route of infection would assume a relatively greater importance.

In connection with the two groups of primary infection through the respiratory and digestive tracts we have a third large group, where the tuberculous changes have their seat in both of these regions but where the extent of the changes does not permit a decision as to the primary seat.

Of the 24 cases in this class (20.5 per cent), those in which death was due to tuberculosis are naturally most difficult to judge as the changes here were greatest. In looking at the 19 cases of this kind it is seen that the question generally is of infection either of the respiratory or the intestinal tract (13 cases), the mouth and throat with their lymph nodes coming into consideration, much more rarely (six cases). In about two-thirds of these cases a primary infection of the respiratory tract must be assumed if we consider the extent of the pathological changes. One point must be emphasized: even when the thoracic organs are found

most affected at autopsy the clinical history may point either to early involvement of the cervical nodes and a descending infection of the throat, or to preceding intestinal infection of long duration.

To the cases of fatal tuberculosis four latent cases must be added, as in three cases the nodes in the chest were involved together with the cervical nodes, and in one case together with the mesenteric nodes; finally one case of latent tubercle bacilli in the tracheal and mesenteric nodes. Whether each of these groups was primarily infected, or one from the other, cannot be definitely determined. The former alternative appears most likely, especially on account of the finding of tubercle bacilli in the different nodes.

The small group of eight cases of tuberculosis of bones, joints etc., and also of lymph nodes (in the chest or neck) will not be given detailed attention. Evidently the lymph nodes here most frequently represent the primary focus from which the other organs were attacked, most likely by hematogenous infection.

On the other hand we must devote some further attention to the generalized tuberculous affections of lymph nodes. There were not less than 11 of these cases (9.4 per cent), five in cases of fatal tuberculosis (miliary tuberculosis, meningitis, etc.), five cases of latent generalized lymph node affections (as a rule caseation in the various groups; in one case only demonstrated microscopically, not by inoculation), and finally a case of latent tubercle bacilli in all the chief groups.

Here the question is raised: are the different groups infected separately, about simultaneously or at different times, and through their respective mucous membranes, or have we to deal with infection of only a single group from which the others are attacked so rapidly and violently as to give the appearance of a general infection?

That it may occur in the former manner we have already mentioned in discussing cases of advanced tuberculosis of both the respiratory and digestive tracts. This explanation is the more plausible in cases in which the changes are little advanced and located in lymph nodes which do not directly communicate. The

same is true of cases in which only latent bacilli in two or more groups are found.

In certain cases, however, we cannot deny the possibility of hematogenous infection of a large part of the lymphatic system. The lymph nodes seem to be a favorite location for the tuberculous virus also in cases of hematogenous infection. This is well known to be so in the certain cases of congenital tuberculosis in man and animals.[1] It is then natural to assume a similar mode of infection in certain cases, especially in the first months of extra-uterine life.

As often, and probably much oftener, the infection spreads from a certain primary focus to the other groups. The most frequent findings are the following: Swollen and generally caseous nodes beneath the lower jaw, and along the entire neck (generally decreasing in size downward), sometimes also in the supraclavicular and axillary regions and, further, in the posterior mediastinum along the trachea, in the pulmonary hilus, and outwards along the bronchi; finally in the mesentery and retroperitoneal tissue from the diaphragm downward along the spine and iliac vessels, and sometimes extending to the inguinal regions. Apparently the affection everywhere is equally advanced, equally old. Such an extension may take place in many ways. The one most commonly thought of is extension from the nodes within the chest in various directions, both because these nodes, according to general opinion, most frequently are found primarily attacked, and because not rarely the affection in this locality appears more marked and perhaps older than in the other localities. Accordingly, the nodes in the hilus of the lung, in the bifurcation of the trachea, and along the trachea most likely have been primarily infected, and from here the infection has spread outward along the bronchi, upward along the trachea to the neck (where, however, the nodes situated highest up very often are most affected),[2] finally downward in the retroperitoneal tissues, and from here to the

[1] The localization of congenital tuberculosis of man and animals is also remarkable. The lymph nodes especially affected are the periportal, retroperitoneal, and bronchial nodes.

[2] Naturally those cases must be left out of consideration where rupture into bronchi has taken place, in which the cervical nodes may be infected from the mucous membrane of the throat by tuberculous expectorate, which is known to take place regularly.

mesentery and along the iliac vessels, etc. Extension from the thoracic to the retroperitoneal nodes is often very plain and conspicuous. This mode of extension is, in fact, quite frequent. However, the point of origin may also be in the cervical nodes. In that case we generally find enlarged nodes along the entire neck, generally decreasing downward; then the supraclavicular and axillary nodes (very generally, as in surgical experience) are attacked, the process descending further to the posterior and anterior mediastinal and other thoracic groups, and finally to the retroperitoneal and other abdominal nodes.

Even where the entire clinical picture decidedly points to a descending cervical lymphatic tuberculosis and where the swelling decreases downward to the clavicle, one finds, as a rule, that it then again increases downward to the hilus of the lung. From this finding one might be inclined to deny the assumption that the thoracic nodes were secondarily involved and maintain that they either were infected separately (from the respiratory tract), or even that they were the starting point. But, in my opinion, this is scarcely correct. The whole evolution often points so decisively to a continuous process, and to extension from above downward, that an interpretation on that basis must be accepted. The marked swelling and pronounced cheesy degeneration of the hilus and tracheal nodes must then be explained by the consideration that these nodes are large, numerous, and perhaps also predisposed to marked swelling. Much seems to point in this direction; at any rate one hardly is justified in denying a continuity in the process even if there is an appreciable diminution in the size of the cervical nodes from above downward and in that of the thoracic nodes from below upward.

Grawitz[1] has also maintained the importance of a descending tuberculosis from the tonsils and cervical nodes to the tracheal and bronchial nodes and finally attacking the lungs. Aufrecht, Beckmann,[3] and others also lay the main stress on infection of the[2] tonsils.

[1] *Deutsche med. Wchnschr.*, 1901, 27. p. 711.

[2] *Verh. d. deutsch. path. Gesellsch.*, 1902, 4, p. 65.

[3] *Das Eindringen der Tuberculose und ihre Bekämpfung*, 1904.

Finally, one may have an ascending tuberculosis from the abdominal lymph nodes to the chest. The infection, which in such cases probably has taken place through the intestinal mucosa, first attacks the mesenteric nodes and extends to the retroperitoneal nodes and further to the various groups situated in the chest and neck. Up to the present time this route of infection has received little attention; in all likelihood, however, it is much more frequent than is commonly supposed. The frequency of latent tuberculosis of the mesenteric nodes, which has been demonstrated mainly by the English authors previously named and by Heller and his pupils, is suggestive in this connection, as are the recent findings of a Norwegian investigator, Hans Thue, who systematically examined the mesenteric nodes of children. It is notable that the more the investigations have been aimed at this mode of infection the more frequent have been the positive results. Numerous animal experiments also point this way, for instance, the highly interesting feeding experiments recently related by Weber and Bofinger.[1] On feeding tubercle bacilli from chickens to rabbits, mice, and guinea pigs the intestinal follicles, mesenteric and submaxillary nodes were first infected; after seven weeks the lungs became involved, and in the third month the bronchial nodes, etc. In the interpretation of these cases of disseminated lymphatic tuberculosis on the basis of extension from a single group we come to a cardinal point:

Can a pathological process, as we here have supposed, really pass from one group of lymph nodes to another? Or, on the contrary, does not each organ possess its definite lymphatic organs which are not connected with each other, but isolated?

This is a question of the greatest interest also in general pathology, in connection with the spread of various morbid processes, especially inflammatory conditions and tumors. It may be stated that although tuberculous inflammation, like many other morbid processes, is prone to remain localized within a certain part of the lymphatic system it has long ago been proved[2]

[1] *Tuberculöse Arbeiten aus d. kais. Gesundheit.*, 1904, 1, p. 83.

[2] C. WEIGERT, in particular, as early as 1884 (*Jahrb. f. Kinderheilk.* 1884, 21, p. 146), emphasized the communications between the lymphatic channels of different regions and their importance in the spread of tuberculous inflammation within the lymph vascular system.

that extension to other groups of lymph nodes and lymph vessels may take place comparatively easily in a direction opposite to that of the lymph current. This occurrence is facilitated when some lymph vessels have become obliterated; the extension will then take place through the capillary communications which exist between the various regions. In the formation of carcinomatous metastasis we also observe an upward extension by continuity through the lymphatics along the spine, subsequently reaching the nodes in the posterior mediastinum and extending further to the neck. Evidence in the same direction is also obtained by inoculating animals with tuberculous material, as has long been recognized, and recently again brought forward by Westerhoeffer (compare also the observations of Weber and Bofinger). The numerous subcutaneous inoculations of guinea pigs, which I have performed in connection with this work, have shown that the infection first has passed to the inguinal nodes, then to the retroperitoneal nodes and to the liver and spleen, thence upward to the posterior mediastinal and hilus nodes and finally to the supraclavicular and cervical nodes. Later the lungs become the seat of scattered tubercles, apparently by lymphogenous infection from the hilus nodes, or perhaps by way of the blood. This is the very route which we previously assumed that tuberculous infection might take in its upward extension from the abdominal cavity. I am quite convinced that infection in man not rarely takes place in this manner, and that as a result not seldom the picture of generalized lymphatic tuberculosis is obtained.

In the discussion of the locations invaded by tubercle bacilli we have started from the generally assumed belief that we may conclude from the localization of tuberculosis in certain definite lymphatic groups that the infection took place through the corresponding organs with their mucous membranes. This may also be accepted as the general rule and is supported by much pathological experience. It is, however, doubtful whether it always holds true. This question has become one of importance within the last few years since the claim has been made by v. Behring that most cases of tuberculosis in adults are attributable to infection in infancy and through the digestive tract irrespective

of the location of the later and most marked pathological changes. In discussing this matter we must first of all direct our attention to children infected during the first year, and especially during the first months of life. It appears to be the case—and of this I have become more strongly convinced the more I have occupied myself with this subject—that tuberculosis readily and rapidly invades the body of the child and quickly reaches those organs which we know from experience to be especially prone to tuberculous inflammation, namely the lymph nodes. One gets the decided impression that tuberculosis relatively easily finds its way to the various lymph nodes.

Most frequently the extension appears to be by the lymph stream but the tendency in children to rapid and frequent infection of the internal organs and to generalization of the tuberculosis also points to the blood stream as a frequent route; and as the lymph nodes, as often emphasized, must be considered especially susceptible, there is nothing against the assumption that they have been infected by way of the blood.

It is also of great importance to bear in mind that nothing appears to be in the way of assuming that tubercle bacilli may pass through one or more groups of lymph nodes before they become stationary and set up inflammation. Thus, nothing appears to me to prevent us from believing that tubercle bacilli may pass through the intestinal mucosa and not cause tuberculous changes until the retroperitoneal, or even the thoracic, lymph nodes have been reached. As stated, feeding of tuberculous material to animals has been known to produce tuberculosis of the nodes in the chest without simultaneous tuberculous lesions in the abdomen. Tubercle bacilli sometimes have been demonstrated in the thoracic duct shortly after the feeding.

If future investigation shall determine that the presence of latent tubercle bacilli is of frequent occurrence also in the mesenteric nodes, then the assumption would be considerably strengthened that the thoracic organs also may be infected by this route. It is shown by clinical observation that tuberculosis of the lungs and thoracic lymph nodes sometimes is preceded by enteritis of long duration. Positive assertions,

of course, cannot be made on this point, as one cannot clinically follow the course of successive swelling of the abdominal groups of lymph nodes.

This route of infection, however, ought to be borne in mind, and especially when the mesenteric and retroperitoneal lymph nodes and the thoracic viscera are diseased.

This question, on the whole, centers about the lymph nodes in the chest. Here another route which we have previously touched upon, comes into consideration, namely, a descending tuberculous infection from the cervical nodes. We have already argued in favor of the extension of a real tuberculous inflammation from the cervical to the thoracic nodes. But we cannot ignore the assumption that in certain instances tubercle bacilli which enter the cervical nodes (where they are quite frequently demonstrated as latent bacilli) may migrate to the nodes in the chest and there cause definite tuberculous lesions. It is sometimes observed that the disease begins with swelling of the cervical nodes which later decreases; the swelling extends downward along the cervical nodes, and later becomes associated with phenomena on the part of the thoracic lymph nodes and the lungs. In such a case one is hardly mistaken in assuming that a descending infection has taken place.

On the whole I believe that it must be admitted that in children as well as in adults a tuberculous infection as a rule is attended with local changes in the corresponding lymph nodes, but at the same time it must be emphasized that dissemination may take place rapidly and easily to the different systems of organs through the different natural vascular systems without the localization apparently being of particular importance.

THE FREQUENCY OF TUBERCULOSIS IN ADULTS.

As stated in the introduction, the work on tuberculosis in children gradually led me to consider tuberculosis in adults, its connection with the disease in childhood and its primary localizations, especially in the lymph nodes and intestines. Originally attention was mainly directed to the two latter points, but this gradually led to a search for tuberculous changes in general in the entire autopsy material. As, however, these investigations

strictly were beyond the scope of my research aud have been made somewhat desultorily by myself and my assistants we have not reached as high figures regarding the frequency of tuberculosis in adults as would be the case if we had been concerned exclusively with that side as were other investigators (Bugge, Nägeli, Lubarsch, Schmorl, Burkhardt, etc.). However, as my figures in their main features agree with those of others and serve to illustrate certain points I think they ought to be given.

For comparison I will first summarize the results from the four preceding years, 1897–1900, when no special effort had been made to demonstrate latent or obsolete tuberculous foci.

TABLE VI.

Year	Autopsies in Adults (over 15 years)	Without Tuberculosis	Total Number with Tuberculosis	Cases in which Tuberculosis caused Death	Cases with Latent and Obsolete Tuberculosis	Cases with Progressive Tuberculosis
1897....	169	68=40.2%	101=59.8%	43=25.5%	46=27.2%	12=7.1%
1898....	200	100=50.	100=50.	45=22.5	43=21.5	12=6.
1899....	195	102=52.3	93=47.7	35=17.9	48=24.6	10=5.2
1900....	172	91=52.7	81=47.2	44=25.6	27=15.7	10=5.9
Total..	736	361=49.05%	375=50.95%	167=22.7%	164=22.3%	44=5.95%

It is seen that here the number of cases of latent and obsolete tuberculosis is very small.

Table VII illustrates the distribution of the different tuberculous changes at different periods:

TABLE VII.

Age	Autopsies	Without Tuberculosis	With Tuberculosis	Cases in which Tuberculosis caus'd Death	Cases of Obsolete Tuberculosis	Virulent Tuberculosis
16-20.....	72	28=38.9%	44=61.1%	30=41.6	4	10
21-25.....	87	30=34.3	57=65.5	39=44.9	16	2
26-30.....	80	36=45.0	44=55.0	31=38.8	12	1
31-35.....	71	30=42.3	41=57.7	21=29.6	14	6
36-40.....	70	37=52.9	33=47.1	12=17.1	14	7
41-45.....	52	30=57.7	22=42.3	8=15.4	13	1
46-50.....	74	39=52.7	35=47.3	10=13.5	18	7
51-55.....	54	39=72.2	15=27.8	4= 7.4	9	2
56-60.....	52	28=53.8	24=46.2	7=13.5	14	3
61-65.....	44	22=50.0	22=50.0	0	21	1
66-70.....	26	12=46.2	14=53.8	4	9	1
71-75.....	21	12=57.2	9=42.8	1	8	0
76-80.....	19	8	11	1	10	0
81-85.....	4	1	3	0	2	1

In certain respects the recorded findings are different in the years 1901–3, during which the investigations of tuberculous children were made. Altogether 537 adults (over 15 years) came to autopsy, divided as follows:

TABLE VIII.

	Autopsies in Adults	Without Tuberculosis	With Tuberculosis	Fatal Tuberculosis	Latent and Obsolete Tuberculosis	Progressive Tuberculosis
1901	169	49=29 %	120=71 %	36=21.3%	78=46.2%	6=3.5%
1902	203	64=31.5	139=68.5	52=25.5	73=36	14=7
1903	186	59=31.7	127=68.3	36=19.4	81=43.5	10=5.4
Total..	558	172=30.8%	386=69.2%	124=22.2%	232=41.6	30=5 4%

Table IX gives the distribution at different ages as to number of cases and in percentages based on the total number of deaths in each class:

TABLE IX.

Age	Autop-sies	Without Tuberculosis	With Tuberculosis	Died of Tuberculosis	Obsolete Tuberculosis	Virulent Tuberculosis
16–20.... ...	65	18=27.7%	47=72.5%	29=44.6%	16=24.6%	2= 3.1%
21–25.....	65	19=29.2	46=70.8	30=46.2	15=23.1	1= 1.5
26–30.....	57	20=35.1	37=64.9	18=31.6	17=29.8	2= 3.5
31–35.....	43	15=34.9	28=65.1	9=20.9	17=39.5	2= 4.7
36–40.....	49	15=30.6	34=69.4	11=22.4	19=38.8	4= 8.2
41–45.....	52	20=38.5	32=61.5	8=15.4	22=42.3	2= 3.8
46–50.....	49	18=36.7	31=63.3	2= 4.1	25=51.0	4= 8.2
51–55.....	44	17=38.6	27=61.4	5=11.4	20=45.5	2= 4.5
56–60.....	37	9=24.3	28=75.7	3= 8.1	22=59.5	3= 8.1
61–65.....	33	11=33.3	22=67.7	6=18.2	15=45.5	1= 3.0
66–70.....	30	3=10.0	27=90.0	0	23=76.7	4=13 3
71–75.....	22	5=22.7	17=77.3	2	12	3
76–80.....	7	2=28.6	5=71.4	0	5	0
81–85.....	1	0	1	0	1	0
86–90.....	3	0	3	0	3	0

The following chart shows these results as far as these figures can be represented in curves, *i*, *e.*, until the figures become too small to be graphically represented.

As is seen, the curve of deaths from tuberculosis in different five year periods is highest at the ages of 16–20 and 21–25 years, the figures here reaching 46 per cent of all deaths. Later the curve rapidly and evenly declines, the minimum death-rate of four

per cent being reached in the period 46–50 years, slightly rising again at the age of 60 to 70.

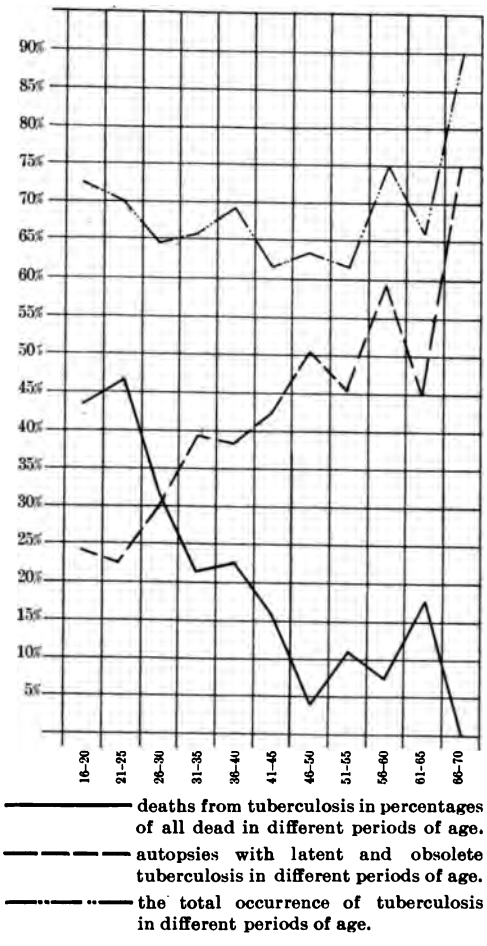
The curves of the latent and obsolete cases show quite opposite conditions, being lowest at the ages between 16 and 25 years (23 per cent). Later it rises rapidly and at 31–35 years reaches 40 per cent, at 55–60 about 60 per cent, and at 66–70 about 77 per cent.

When all tuberculous changes put together are represented by one curve it begins comparatively high at the age 16–20, with 72.5 per cent, then sinks somewhat to the forties (61.5 per cent), again rising rapidly in the sixties, where it reaches 90 per cent.

In connection with these curves it must be remarked that the absolute numbers from which the percentages have been computed are quite small between the ages of 60 and 70. On the whole, however, these curves must be considered correct expressions of the relationship of fatal tuberculosis on the one hand and of the latent and obsolete forms on the other hand at various ages.

CHART I.

FREQUENCY OF TUBERCULOSIS IN ADULTS.



As we see, the figures for the years 1901–1903 are considerably higher than those of the preceding period 1897–1900, and

the increase is due to the much larger number of latent and obsolete[1] cases included, while the number of those who died of tuberculosis is about the same and in accordance with the mortality of tuberculosis in the entire country. Yet, several cases may have escaped attention while all those included may be considered as certain. The cases with only pleural adhesions, small cicatrices and indurations in the lungs without pultaceous or caseous foci, plaques of thickened pleura over the apices, etc.—changes often noted in the autopsies, have not been included. Moreover it must be remembered that microscopic examination of doubtful foci was only exceptionally made. If we also consider that negative findings have been recorded in cases with non-tuberculous lesions in the lungs, such as pneumonias, tumor metastases etc., it may be concluded that the figures quite certainly ought to have been greater. Arbitrarily, I believe, the percentage of tuberculous changes might have been brought up to 75 or 80 or more.

By way of comparison, it is of interest to recall the figures obtained by another Norwegian observer, J. Bugge,[2] which are based on extremely exact observations. Bugge obtained about the same figures; his classification of the various tuberculous changes, however, is somewhat different.

In 200 autopsies of individuals over 14 days old (21 under one year and 22 from one to nine years) Bugge, who exclusively directed his attention to the lungs and bronchial nodes, found tuberculous changes in 136 cases, or 68 per cent while 64 or 32 per cent were free from tuberculosis of the lungs and bronchial nodes. Of the 136 cases, in 42 (21 per cent) death was due to tuberculosis, in 45 (22.5 per cent) there was virulent tuberculosis (demonstrated by inoculation of guinea pigs), and in 49 (24.5 per cent) obsolete, healed tuberculosis.

The difference between Bugge's statistics and mine will be noted. In my tables for the years 1901–3, cases of developing tuberculosis, *i. e.*, virulent and progressive tuberculosis, have been grouped together, and in another group have been placed the cases of latent and obsolete (always encapsulated) tuberculosis, which constitute the bulk of the whole number. This was necessary as I did not make inoculations, and hence could not decide what latent foci did or did not contain virulent bacilli. The question whether in Christiania conditions are such as to be correctly represented by Nägeli's figures, according to which practically all adults show traces of tuberculosis, I shall leave unanswered. However, it appears unlikely to me, as we occasionally

[1] As latent we have considered those cases in which the process had not been completed and where we must suppose that virulent bacilli still exist. As obsolete we have considered cases of healed tuberculosis with contracted scar tissue, calcification, etc.

[2] *Undersögelser om Lungetuberkulosens Hyppighed og Helbredelighed*, 1896. Bugge made microscopic examination and inoculation of guinea pigs in all doubtful cases.

meet with cases in which the most searching examination fails to reveal tuberculous changes.

For comparison the statements concerning the frequency of tuberculosis in certain more extensive recent works will be given.

Nägeli[1] in his first series found 75 per cent, later 90 per cent of tuberculosis in adults (over 17 years), but in his most recent series the percentages rose to 97 and 98. In his last 284 autopsies there were only six in which no trace of tuberculosis was found; among these 284 cases there were 63 lethal forms, 74 active latent, 111 inactive latent (healed); 32 were in a very uncertain position.

Nägeli reaches his high figures by including in the inactive latent forms apical pleural adhesions, pleuritic scars with shingle-like indurations, calcified foci in the lungs and bronchial nodes, and combinations of these findings.

Although most of the lesions included probably were tuberculous yet there is doubt in regard to some of the cases, for instance, the shingle-like indurations. This is also partly admitted by himself. The correctness of this objection is also shown by the investigations made by Lubarsch. (See article cited below).

Burkhardt,[2] in his report of 1262 autopsies in adults over 18 years from the pathological institute of Dresden (Prof. Schmorl) also reached very high figures, tuberculosis in some form being present in 91 per cent of the cases. There were 466 cases (41 per cent) of death from tuberculosis, 209 cases of latent active forms, and 474 cases of latent inactive forms. It is seen that it is the very high percentage of lethal cases (41 per cent) which causes the high total of 91 per cent, while the figures in the other two classes about correspond with those of myself and others. On account of this anomaly, which is supposedly due to the material Burkhardt's figures cannot be compared directly with the others.

According to Hof's[3] account of 15,000 autopsies from Kiel, tuberculosis was found in only 2,697 of the 7,683 autopsies in adults (35.1 per cent).

Lubarsch, in his interesting work previously mentioned, obtained considerably higher figures. There were about 1,820 autopsies (297 in children), and tuberculous changes were found in 1087 cases, and, if some (about 10 per cent, of the shingle-like indurations are included, in 1,106 cases (60.6 per cent) On deducting persons under 10 years we have tuberculosis in 1,040 out of 1,522 cases, or in 69.1 per cent, which is quite close to my result. Among the 1,087 cases there were 515 (47.4 per cent) of florid tuberculosis, 485 (44.6 per cent) absolutely healed, and 86 (7.9 per cent) almost healed — the last two groups together constituting 52.5 per cent. These figures also correspond quite well to mine.

It is still too early to express one's self as to what might be considered the usual percentage of tuberculosis in the dead. The figures of Lubarsch and myself perhaps are too small; however, I believe on the other hand that those of Nägeli and Burkhardt are

[1] *Virch. Arch.*, 1900. 160, p. 426–472.

[2] *Münch. med. Wchnschr.*, 1903, 29, p. 1275.

[3] *Loc. cit.*

too high. Some autopsies always will occur in which no trace of tuberculosis is found no matter how careful a search is made, even where microscopic examinations and inoculations as made by Bugge, are employed. Otherwise it may well be that conditions vary greatly in different places.

THE PRIMARY LOCALIZATION OF TUBERCULOSIS OUTSIDE THE RESPIRATORY TRACT IN ADULTS, WITH SPECIAL REFERENCE TO ITS OCCURRENCE IN LYMPH NODES AND IN THE INTESTINAL TRACT. TUBERCULOSIS OF LYMPH NODES IN ITS RELATION TO PULMONARY TUBERCULOSIS IN ADULTS.

I wish first to consider my experience with tuberculosis in adults in the years 1897–00, *i. e.*, before the inauguration of systematic study of the entire material. It seemed little likely that much of interest would be found in this material, yet many cases elucidate lymphatic tuberculosis in general as well as its mode of extension and duration. Hence some examples of the more characteristic forms are worth including.

On perusing the records of the 375 cases from the years 1897–00 in which tuberculosis was found (51 per cent), and in 167 (22.7 per cent) of which death was from tuberculosis, I find only nine cases in which there is a history of enlarged lymph nodes in childhood, remnants of which, at times, were found at autopsy in the form of scars on the neck. This figure naturally is much too small, as this condition is not always looked into and information concerning it not always recorded in the clinical history. In six of the nine cases no connection between these enlarged nodes in childhood and the subsequent pulmonary tuberculosis could be demonstrated anatomically, as there was no trace of a progressive lymphatic tuberculosis, the pulmonary tuberculosis apparently having developed as a primary disease. In the three other cases, on the contrary, there was quite an extensive, in all probability primary, lymph node tuberculosis, in two cases chiefly located in the chest and giving rise in the one case to miliary tuberculosis, in the other to pulmonary tuberculosis.

In regard to the third case, that of a woman 24 years old, it was stated that when quite little she had "glands in the eyes," at ten "glands in the stomach," and at thirteen "glands in the neck,"

and that she was operated on for the latter affection at 18. She died at 24 after an illness of half a year. Aside from comparatively recent pulmonary tuberculosis and small intestinal ulcers, there was quite marked tuberculosis of the lymph nodes which were enlarged to walnut-size, caseous, and partly calcified; the disease was most marked in the thorax (tracheal and hilus nodes) and in the mesentery.

The lymph node affection may here quite certainly be considered primary, and the clinical history would suggest a primary descending tuberculosis of the cervical nodes.

Otherwise, in the 17 cases (plus the three cases just mentioned) there was a primary and a well advanced tuberculosis of the nodes in the chest (especially in the tracheal and hilus nodes) with secondary tuberculosis in other organs, viz., miliary tuberculosis in nine cases, sometimes most prominent in the lungs, tuberculosis of the serous membranes in two cases, and in the other six cases secondary pulmonary tuberculosis. (I leave out the numerous instances of latent and obsolete lesions of the thoracic nodes.)

To these must be added two cases of extensive, almost general, lymph node tuberculosis (in one case mainly abdominal, perhaps primarily so; it will be considered later) with secondary pulmonary involvement. The affection of the lymph nodes was here very marked and old, most of the nodes being caseous, while the pulmonary lesions were relatively recent.

Thus we have 12 cases of pulmonary tuberculosis in which we have every reason to look upon it as secondary, it having appeared subsequently to, and probably from, tuberculous nodes.[1] In a few cases perforation from bronchial nodes to the bronchi was demonstrated, in others the pulmonary tuberculosis must be looked upon as of lymphogenous or hematogenous origin, of the latter especially when the original seat was extrathoracic.

If six cases of primary involvement of the mesenteric and retroperitoneal nodes and finally one case of primary tuberculosis of the axillary and cubital nodes are added it will be seen that primary lymph node tuberculosis is quite frequent in adults

[1] In addition there were cases of small encapsulated foci in the lungs in connection with primary tuberculosis of other organs, to be referred to later.

—altogether 28 cases—and that its rôle is quite important as it most frequently causes death from secondary tuberculosis of vital organs. Most of these cases, therefore, belong to the 167 fatal cases, comprising about 15 per cent.

Certain cases merit brief narration:

Autopsy 176, 1899. Woman, aged 45, who one and one-half years before death had repeated attacks of rheumatic pain in the left arm. A year later she noticed swelling of the left cubital and axillary nodes. She died suddenly of pulmonary embolism from thrombosis of the veins in the arm. The autopsy revealed numerous wholly caseous lymph nodes, some of which were of walnut size; they were located beneath the outer end of the left clavicle, whence they formed a continuous chain to the axilla, and also along the entire arm, and at the elbow. There was no wound or scar on the left hand or arm. The tonsils, the cervical, thoracic, and mesenteric nodes were not tuberculous, but a recent peritoneal tuberculosis was present.

The affection of the left axillary and cubital nodes must here be considered primary; how this infection had been brought about remains unknown.

In regard to primary tuberculosis outside the respiratory organs and lymph nodes the conditions for the years 1897–1900 were as follows:

Primary tuberculosis of the genital organs in four cases (in some of these there were small encapsulated pultaceous foci or scars in the lungs or lymph nodes); of the urinary organs in one case; of serous membranes in two cases; of bones and joints in one case; of the skin in one case. In three cases there was tuberculosis of the adrenals, but always secondary, originating in the lungs or bronchial nodes.

The case of primary cutaneous tuberculosis is worth narrating on account of the subsequent descending affection of the lymph nodes.

Autopsy 104, 1898. Man 49½ years old. His wife and one daughter died of tuberculosis; eight years ago he developed lupus of the left ear, later swollen cervical nodes for which he was operated upon several times. Subsequently he developed tuberculosis of the pharynx and ear. He died with cerebral symptoms. Autopsy: In addition to lupus of the left ear there were tuberculous cervical nodes which were enlarged to walnut size and caseous, in part much softened; on the left side these softened nodes are confluent and formed an abcess the size of a pigeon's egg, which extended to the base of the skull. Along the entire trachea and in the posterior and anterior mediastinum there were numerous caseous nodes varying in size from that of a pea to that of a

hazelnut. In the apices of the lungs were several firm consolidated nodules up to walnut size, with caseous and pultaceous foci; also numerous tubercles of the size of a pin head or hemp seed, scattered or arranged in groups. Also tuberculosis of the left middle ear and tuberculous meningitis; one large and several small tuberculous ulcers in the ileum. In the root of the mesentery were several partly softened lymph nodes enlarged to the size of a walnut. Scattered tubercles in the liver, spleen, and kidneys.

It may be supposed that a descending lymphatic tuberculosis originated from the lupus on the left ear; and as the tuberculosis of the lymph nodes appear to be oldest and most pronounced the pulmonary involvement was probably secondary.

The cases of certain or probable primary infection through the intestinal tract must be given special mention. There were five cases, three of which were certain, two somewhat doubtful.

1. In one case (128, '98) there were scars in the small intestine which had to be looked upon as signs of healed and isolated intestinal tuberculosis.

2. In a second case (56, '98) there was a comparatively recent intestinal tuberculosis and also a scar in the apex of one of the lungs. In all probability the intestine had been separately infected and probably considerably later than the lung in which the process was inactive and completely encapsulated.

3. A third case (154, '00) concerned a woman 40 years of age who ten years before death had been operated on for tuberculosis of the wrist. She died of miliary tuberculosis. The autopsy revealed the scar of a tuberculosis of the left wrist (healed after operation); tuberculosis of the lymph nodes in the chest; a few encapsulated caseous foci in the apices of the lungs of the size of grains of wheat; miliary tubercles, especially in the lungs and kidneys; large tubercles of the cerebellum, spleen, and liver; finally large, transverse, old ulcers of the large intestine and caseous mesenteric nodes. The intestinal tuberculosis cannot readily be explained except by assuming a primary infection of the intestine.

4. The following case must be looked upon as one of primary tonsillar and intestinal tuberculosis (39, '99.) A girl, 17 years old, entered the hospital in an unconscious condition and died shortly after admittance. There was miliary tuberculosis of all organs, including the lungs, in which, otherwise, only an encapsulated, caseous nodule, the size of a pea, was found in the right lower lobe. There was a caseous nodule in the thoracic duct. Right tonsil rather large and in an area .5 c.m. wide, coated with yellowish material; it contained masses of tubercles. On the right side of the neck were lymph nodes of the size of beans; one node, of hazelnut size, was caseated: microscopically, masses of tubercles. In the hilus of the lungs enlarged nodes, in part studded with tubercles; there was no continuous chain of nodes along the trachea and neck. In the intestine scattered tuberculous ulcers; in the mesentery enlarged caseous nodes. Beginning tuberculous salpingitis.

The oldest tuberculous changes appear to be in the digestive tract, viz., in the tonsils and, more marked, in the intestines; the

involvement of the latter, at any rate, is not secondary to tuberculosis of the respiratory tract.

5. The following is a pure case of tuberculosis of the intestines and mesenteric nodes (232, '98). A woman, 45 years old, died of fecal fistula. There were large tuberculous ulcers in the cecum and ascending colon, and numerous swollen tuberculous lymph nodes in the mesentery and retroperitoneal connective tissue, especially around the pancreas. No trace of involvement of the lungs. In the hilus nodes, on the other hand, tubercles were demonstrable microscopically.

There were also nine cases in which primary tuberculosis of the mesenteric and retroperitoneal nodes was demonstrated, in three cases associated with involvement of other nodes, but from its appearance older and more marked than the latter affection; in six cases the abdominal nodes only were involved. The lymph nodes attacked were always caseous. In these cases we may assume a primary infection through the intestinal tract, at any rate when the mesenteric nodes were involved; the matter is somewhat more in doubt when the retroperitoneal nodes alone were involved (as was true of three cases, in one of which there was a secondary adrenal tuberculosis).

Of the cases just mentioned only one will be narrated which quite certainly must be looked upon as an ascending affection of lymph nodes originating in the abdomen.

(67, '99.) Woman, 19 years old. At 13 abdominal pain and diarrhea set in, followed by abdominal enlargement and emaciation; the following summer she entered a hospital on account of "glands in the stomach;" she could feel hard lumps herself. After 15 months she left and was quite well. Three months before death abdominal pain recurred and was accompanied by fever. The autopsy revealed both old and recent tuberculous peritonitis. No intestinal ulcers. Very extensive lymph node tuberculosis in the mesentery, retroperitoneal connective-tissue, upward along the spine (a cluster the size of a fist behind the stomach), at the roots of the lungs; bean-sized supraclavicular nodes on both sides; tonsils atrophic. Lungs entirely free from tuberculosis.

We have here a primary lymph node tuberculosis which we must assume to have originated in the mesenteric nodes and to have ascended.

Hence, there were altogether 14 cases (nine certain, five somewhat doubtful) of primary infection of the digestive tract (intestine, abdominal nodes, tonsils). This constitutes only about two

per cent of the total 736 autopsies, and about four per cent of the 375 autopsies in which tuberculous changes had been demonstrated. If to these cases we add those of primary localization outside the respiratory and digestive tracts and some of the primary lymphatic cases, the bulk of the remaining cases depends on primary infection through the respiratory tract, which in the great majority of the cases—at least 90 per cent—is primarily attacked. However, in most of the latter cases, the lesions consist of tuberculous inflammation of lungs and thoracic nodes which is often completely healed. On the other hand, the cases in which the disease originated outside the respiratory tract most frequently terminated fatally and really should be considered together with the 167 cases of fatal tuberculosis. Thus the importance of these cases is enhanced. But, on the whole, the number of recorded cases of primary tuberculosis outside the lungs and lymph nodes in this series is too small; among other reasons because sufficient attention had not been given to detecting such cases.

For the years 1901–03 conditions are decidedly different. During this period the bodies of 538 adults came to autopsy, 124 (or 22.2 per cent) had died of tuberculosis while 232 (or 41.6 per cent) had latent or obsolete tuberculosis.

The number of cases of supposedly primary lymph node tuberculosis here is quite great.

Of primary tuberculosis of the hilus, tracheal and bronchial nodes[1] seven cases were observed, most of which occurred in young persons (ages respectively 16, 17, 17, 17½, 20, 31, 74 years) illstrating the well-known fact that from the age of 15 and a little into the twenties tuberculosis as a rule is a primary lymph node affection. Secondarily this had given rise to miliary tuberculosis (two), tuberculosis of the genital organs (one), of the lungs (one), of bone (one), of serous membranes (two).

There were 10 cases at least—four of them somewhat doubtful—of primary tuberculosis of the cervical nodes with subsequent extension to other lymph nodes and to internal organs the

[1] The numerous cases of small, encapsuled latent or obsolete tuberculous lesions in these nodes are not included.

involvement of some one of the latter being the cause of death in most cases.

Further, there were some cases of generalized tuberculosis of lymph nodes in which the point of origin no longer could be demonstrated; some of the cases appeared to be instances of descending tuberculosis from the throat. In some cases there was tuberculosis in two different groups, the connection of the lesions not being cleared up (in cervical and thoracic nodes or in thoracic and abdominal nodes).

If we also add the cases of isolated or primary tuberculosis of the mesenteric or retroperitoneal nodes the total number of cases of well-marked, primary tuberculosis of lymph nodes will be 30. In most of these cases death was due to subsequent localization in internal organs, so they form a considerable proportion, about 20 per cent of the total deaths from tuberculosis. Herein we must include a small group of six cases in which there was considerable lymph node tuberculosis but also advanced involvement of various internal organs, mainly the lungs so the connection becomes somewhat doubtful.

To illustrate this class I shall narrate several cases, especially of the generally neglected type of progressive tuberculosis of the cervical nodes, and of general tuberculosis of the entire lymph node system. The clinical features will also be briefly stated whenever necessary for the understanding of the evolution of the tuberculous changes.

Case 1. (124, '01.) Girl, 19 years old, died of amyloid disease on June 26, 1901. There was a pronounced family history of tuberculosis. She had bronchitis and twice pneumonia in childhood. From the age of five years there was enlargement of the cervical nodes. At seven diarrhea with painful bloody stools. She was in the hospital from January 1895 to January 1896, and a diagnosis of tuberculosis had been made. There were lumps of the size of a hen's egg in the neck, above the clavicles and in the axillae and groins; also phlyctenular kerato-conjunctivitis. Enlarged liver and albuminuria (amyloid degeneration). Autopsy: Clusters of nodes of goose-egg size on both sides of the neck. Lungs normal. The nodes along the bronchi, at the hilus of the lungs, and along the trachea were somewhat enlarged: in most of them calcareous or pultaceous material was not seen. The mesenteric nodes and — to a lesser degree — the retroperitoneal nodes were enlarged and generally contained pultaceous foci. No intestinal ulcers, but tuberculous salpingitis and endometritis were present. Amyloid degeneration of all organs.

Undoubtedly the lymph node affection here was primary and originated in either the cervical or mesenteric nodes (or possibly, in both groups). The clinical history points to the cervical nodes as the primary seat.

Case 2. (26, '02.) Servant girl, 40 years old; enlarged cervical nodes since the age of one and one-half years. At 23 she was operated on for enlarged glands on both sides of the neck, under the chin, and in both axillae. Later she was apparently well until digestive disturbance set in about a year before death. In March 1901 pain in the ileocecal region and bloody stools suddenly appeared. The autopsy revealed an almost general tuberculosis of the lymph nodes, viz., in the nodes in the lower part of the neck (not the tonsils); along the trachea, increasing downward; in the nodes in the hilus of the lungs (but not in the bronchial nodes), in the retroperitoneal nodes (in hilus of liver and spleen): in the mesenteric nodes, decreasing in size and number toward the intestine (largest and most numerous in the root of the mesentery). The retroperitoneal nodes formed a large mass of pultaceous and caseous nodes, up to the size of a pigeon's egg, which adhered to the duodenum. A large node had caused a narrowing of the lumen of the duodenum (with secondary dilatation of the stomach), and finally had perforated the wall of the duodenum and produced a tuberculous ulcer. No tuberculosis of the nodes in the small pelvis or in the inguinal nodes. No intestinal ulcers (except the one in the duodenum). In the apices of the lungs small encapsulated caseous nodules.

The clinical and postmortem findings here point to a descending affection from the cervical nodes to the tracheal and probably further to the retroperitoneal nodes. The small encapsulated foci in the lungs must be looked upon as secondary, either brought about by hematogenous infection from the lymph nodes, or as having arisen at another time (possibly by inhalation of tubercle bacilli).

Case 3. (72, '02.) Man, aged 30, who at 15 developed enlarged cervical nodes which steadily grew larger and were operated upon. In 1898 one node began to suppurate, and later had discharged pus from time to time. During the winter of 1897–8 he had a prolonged bronchitis, and pleuritis in the summer '99. In December '01 again cough, later hemoptysis; he died April 17, '02. Autopsy: Pulmonary and intestinal tuberculosis of usual appearance (cavities in one apex). Extensive lymph node tuberculosis with greatly enlarged caseous nodes along the neck from the mastoid processes to the clavicles; along the trachea, especially at its bifurcation, in the hilus of the lungs, the retroperitoneal tissues, in the mesentery and groins. The nodes were enlarged to the size of pigeon's eggs, partly softened.

On the basis of the clinical data we may suppose that the affection of the lymph nodes was primary (probably originating in the

cervical nodes), and that the pulmonary tuberculosis appeared later, possibly on the basis of the lymphatic affection.

Case 4. (170, '02.) A woman, aged 21; as a child she had enlarged cervical nodes (which did not suppurate), and chlorosis at 10; otherwise well until two attacks of appendicitis at 19; since then she was not quite well, was especially troubled by constipation, felt weak, and steadily lost in flesh. After the appearance of edema and increasing marasmus she died September 15, 1902. Autopsy; Extreme emaciation; pronounced enteroptosis; also anemia and considerable atrophy of all organs. Bilateral bronchopneumonia. Tonsils small, without scars. Cervical lymph nodes on both sides much enlarged, forming chains of completely caseated nodes from hazelnut to walnut size (a softened few nodes at the back of the neck). They continue downward in both supraclavicular regions; in the posterior mediastinum along the esophagus and aorta where there are shrivelled calcareous or pultaceous nodes of hazelnut size; smaller nodes in the pulmonary hilus (not along the bronchi). In the apex of the right lung three small encapsulated caseous or calcareous nodules. In lower ileum, in the cecum and part of the ascending colon there are old contracted tuberculous ulcers with marked thickening of the intestinal walls and adhesions to surrounding structures. In the mesentery a number of pea-size calcareous nodes; likewise in the retroperitoneal connective tissue above the pancreas, and in the hilus of the liver and the lesser omentum. A direct connection with the posterior mediastinal nodes could not be demonstrated.

The clinical and postmortem findings here are decidedly in favor of assuming an old primary tuberculosis of the cervical nodes, descending to the supraclavicular and posterior mediastinal regions (and possibly to the retroperitoneal nodes). Then the intestinal tuberculosis must be looked upon as an old primary tuberculous affection. The small nodules in the lungs are most probably secondary, due to hematogenous infection in an organism, a whole system of which, namely, that of the lymph nodes, for years had been permeated by tuberculosis. But an independent infection of the lungs by inhalation cannot be excluded.

Case 5. (64, '03.) Man, 23 years old. Mother died of pulmonary tuberculosis, and another of her children had enlarged nodes. At the age of 10 or 11 years he developed enlarged cervical nodes which suppurated from time to time, and persisted; two years ago the nodes on the right side of the neck were operated on. Otherwise healthy. Four months before death cough, pain in the side, and signs of tuberculosis of the thoracic organs. He died April 5, 1903. Autopsy revealed a very extensive tuberculosis, with calcification and caseation, and partial fibrous transformation of the lymph nodes, viz., cervical of both sides, axillary, posterior and anterior mediastinal, hilus and bronchial, retroperitoneal and mesenteric. Also tuberculosis of lungs and pleurae, and finally miliary tubercles in spleen, liver, and kidneys.

It may be assumed with certainty that the lymph node affection was primary, descending from the neck to chest and abdomen. Probably the origin of the pulmonary tuberculosis also lay here; but it may also have arisen independently and later, in another manner (inhalation?).

Case 6. (111, '04.) Woman, aged 48, who died of amyloid degeneration and extensive thromboses. As a child she had scarlet fever, measles, and "glands of the neck" (not suppurating). At 36 repeated attacks of cholecystitis. Four years before death bronchitis set in. The autopsy revealed an old tuberculosis of the cervical nodes. Below angle of right jaw an almond-sized completely fibrous node with a pultaceous focus in its middle. Outward, along the right side of the neck to the clavicle there was a continuous fibrous lymphatic chain with a row of hard, partly pultaceous nodes up to bean size. Similar nodes along the trachea, in the hilus pulmonis (no large ones at bifurcation), along the bronchi. Old pulmonary tuberculosis with cavities having smooth lining and surrounded by indurated fibrous tissue. No intestinal ulcers. Mesenteric nodes small, greyish red, soft.

The clinical history in connection with the postmortem findings point to descending tuberculosis of the cervical nodes, and it seems natural to consider the pulmonary affection as dependent on it; but it might also have arisen independently later.

Case 7. (210, '91.) Woman aged 19, who died after an illness of about six weeks. The disease behaved like a serious infection (as typhoid fever or pyemia), with continuous high fever (temperature 100.4° to 104.5° F.) and increasing marked anemia. The autopsy revealed extensive and advanced tuberculosis of the lymph nodes, especially along the whole spine, viz., in those in the posterior mediastinum, along the trachea, in hilus pulmonalis, along the bronchi, in the retroperitoneal, iliac, inguinal (size of pigeon's egg), and mesenteric nodes, the latter decreasing in size toward the intestine. The nodes were completely caseous, in part softened; the posterior mediastinal and retroperitoneal partly calcified. The axillary and cervical nodes were comparatively little swollen. There was rupture of a bronchial node into a bronchus leading to the right middle lobe, in which scattered tuberculous bronchopneumonic foci were seen. Tubercles here and there in the spleen and liver. No tuberculous ulcers in the intestines.

The disease of lymph nodes must be considered primary, that of the lung secondary. It cannot be settled whether the lymph node affection originated in the thoracic or abdominal nodes. The clinical picture with anemia and prolonged fever is of great interest.

Case 8. (127, '02.) Man, 56 years old, who died with a peculiar clinical picture; no information about "glands." The autopsy revealed large masses

of tuberculous nodes in the abdomen (retroperitoneal and mesenteric), along the entire trachea and in the posterior mediastinum, and also on both sides of the neck; the nodes were walnut- to pigeon's egg-sized and caseous. In one apex a cicatricial nodule with small calcareous and pultaceous deposits; in the liver numerous large tuberculous nodules.

The lymph node affection is very old; whether primary in the neck, chest, or abdomen cannot be decided.

Case 9. (129, '02.) Man, aged 43, of a tuberculous family. Symptoms of pulmonary tuberculosis for one year; a mass had been felt in the abdomen. Autopsy: Pulmonary tuberculosis with cavities. Also a continuous mass of large caseous lymph nodes in the mesentery, retroperitoneal tissues, posterior mediastinum, along the trachea and in the neck. Apex of left lung (and partly that of the right) surrounded by and embedded in a mass of caseous nodes, which were partly soft, partly hard, and enlarged to the size of a pigeon's egg. A few small recent tuberculous ulcers in the intestine. Scars on the neck. Tonsils normal. Very large and caseous inguinal nodes.

The affection of the nodes is at least very old; comparing it with the lung findings, it seems likely that the disease began in the lymph nodes. The scars on the neck point to the existence of an old tuberculosis of the cervical nodes.

Case 10. (152, '02.) Woman, aged 63, who had suffered for about one and one-half years from an itching skin disease, with infiltrations of the skin and desquamation (diagnosed by Professor C. Boeck as dermatitis exfoliativa universalis);[1] gradually marked enlargement of all lymph nodes appeared, bronchitis (without tubercle bacilli in the sputum), slight febrile attacks; finally diarrhea (no abnormalities in the blood). Died August 23, 1902. Autopsy: skin everywhere spotted, grayish brown, mostly smooth, in places desquamating; the spots vary in size from that of a hemp seed to that of a pea. Dr. Bruusgaard succeeded in demonstrating tubercles and tubercle bacilli in the spots. There were bronchitis and bronchopneumonia, but no sign of tuberculosis in the lungs. The lymph nodes at the root of the lungs were of hazelnut size, as were the mediastinal, axillary, and cervical nodes of both sides; some of the nodes were three to four c.m. long, 1.5 c.m. broad, soft, some of them almost broken down, with greyish white cut surface, on which numerous small yellow necrotic foci were seen. The mesenteric nodes were comparatively little enlarged, the retroperitoneal and inguinal nodes, on the other hand, enlarged (to the size of a pigeon's egg), and with small necrotic areas. A small ulcer in the ileum. On microscopic examination tubercles were found in the liver and spleen, and in the lymph nodes an atypical tuberculous granulation tissue rich in tubercle bacilli.

We have here an almost general tuberculosis of the lymph nodes and of the skin. Which is primary is not easy to state,

[1] The case has been described by Dr. Bruusgaard in *Norsk Mag. f. Laegevid*, 1903, 5, R. i. p. 156.

though probably that of the lymph nodes. Whether the latter affection was general from the outset or commenced in a certain region cannot be determined.

On perusing the cases just given,[1] one is compelled to admit that the primary localization of tuberculosis in adults frequently is in the lymph nodes, and that this form often has an extremely chronic course, with pronounced tendency to extension from place to place, from one group to another, and ultimately in the course of many years is prone to become almost general. Naturally, doubt will exist as to the conception of many of these extensive or general affections of lymph nodes. My opinion, as based on the combined postmortem and clinical findings, has been given in the epicritical remarks accompanying each case, and I find no reason to enter into further discussion of each case.

It is, on the other hand, necessary, on the basis of the entire material, to make a few remarks as to the localization and mode of extension of the infection in these cases in general. The explanation here can be in one of three directiens (compare what has been said in connection with tuberculosis in children):

1. Large portions of the lymph node system may be infected simultaneously with tubercle bacilli brought by way of the blood channels and deposited in the lymph nodes as localities predisposed to infection. The cases of fairly evenly distributed tuberculosis of lymph nodes without coexisting changes in the internal organs, especially in the mucous membranes, are the ones which might invite such interpretation. (Some are found among the 10 cases, for example, Nos. 8, 10, etc.) The infection might then be imagined to have taken place before birth through the placental circulation, and this possibility cannot be excluded, especially in cases of young persons with tuberculous affections dating back to the first years of life, and perhaps particularly in cases in which the chief localization is in the lymph nodes of the hilus of the liver, the retroperitoneal nodes, etc. Or, the

[1] It is also well to bear in mind certain cases from the years 1897-1900, such as 39, '99 (tuberculosis of tonsils and cervical nodes); 110, '00 (old tuberculosis of cervical nodes); 104, '98 (lupus with descending lymph node tuberculosis); 67, '99 (ascending tuberculosis from the abdomen). In the following some of the cases of intestinal tuberculosis, Nos. 6, 7, and 8, will also be taken into consideration.

infection may have taken place post partum, a considerable number of tubercle bacilli having entered the blood stream (directly or after first having passed part of the lymph vascular system) through some organ or some mucous membrane, without having left any demonstrable changes, or at least only changes so small as to be generally overlooked. This mode of infection I believe to be rare, but it well deserves to be considered.

2. It may be supposed that infection of the different parts of the lymph node system has taken place separately, either simultaneously or at different times. This explanation is quite certainly the correct one in a number of cases, especially where the affection is not pronounced in the different groups, where the nodes involved are not directly connected, and also in cases in which the lesions plainly vary in age; for instances, in one group encapsulated, pultaceous, and calcareous foci, in other groups recent eruption of tubercles (perhaps only microscopic). On the whole, attention, much more than formerly, must be directed to repeated infection at different times of different organs, or even of the same organ. With my experience in view I must, in this respect, quite agree with Lubarsch and Ribbert, who recently have maintained the same thing. This explanation is especially applicable in cases of coexisting tuberculosis of the cervical nodes (+ tonsils), and in the intestine with the mesenteric nodes, as well as in coexisting slight tuberculosis of cervical and thoracic nodes or of thoracic and abdominal nodes.

3. The third mode is a successive extension from a single place to the neighboring groups of lymph nodes until a greater portion of the lymph node system of the body is the seat of a tuberculosis, which, while of different age, is of about uniform appearance. This mode I consider particularly frequent and, therefore, will call special attention to it. In arriving at such a conception of a given case, however, the postmortem findings do not suffice, but an exact clinical history, with clear exposition of the main points in the development of the disease, is also essential. This is particularly true in cases of supposed primary localization in the cervical and mesenteric nodes, which, so far as my experience at present goes, very frequently shows a tendency to continued

further extension. The correctness of this will appear from the cases given, the first of which are especially instructive in regard to extension from the cervical nodes and which also (like the following cases of intestinal tuberculosis) contains instances of extension from the abdominal nodes.

With all these cases in mind there is no room for doubting the correctness of the view which I also maintained in connection with tuberculosis in children, that tuberculosis of the cervical nodes may descend to the nodes of the chest and abdomen, finally to become almost general, and, conversely, that tuberculosis of the abdominal nodes may ascend to chest and neck, and, finally, that tuberculosis of the thoracic nodes may extend upward and downward to neck and abdomen respectively, and also along the bronchi. As long ago maintained by Weigert, I consider the communications between the lymph nodes of different regions as amply sufficient to explain such extension. Observations in regard to extension of malignant tumors, especially carcinoma, and results of experiments on the transmission of tuberculosis to animals also confirm this. It is noteworthy that the infection generally seems to extend continuously, without leaps. It is another matter that we find the affection most marked in certain localities possessing numerous and large lymph nodes, *e. g.*, the upper part of the neck, the bifurcation of the trachea, the hilus of the lung, the retroperitoneal connective tissue behind the stomach, about the pancreas, etc.

The results of the findings in the cases narrated and of considerations called forth by them warrant the following conclusions:

First, that primary tuberculosis of lymph nodes is quite frequent in adults.

Second, that besides in the thorax tuberculosis is quite often primary in the abdomen and especially in the cervical nodes.

Third, that not seldom it is found generally distributed, and

Fourth, that it often extends from one place to another, during years or dozens of years, so that finally a great portion of the lymph node system has been attacked by tuberculosis.

In this connection the question of the duration and latency of such tuberculosis is raised. We must disregard the possible

occurrence of latent tubercle bacilli in the lymph nodes of adults as no special investigations have been made on that point. From the experience in children and the result of experiments concerning the occurrence of latent tubercle bacilli in adults, which have previously been related, it appears reasonable, however, that here also such infection, without demonstrable anatomical changes, might frequently be demonstrated, and that tubercle bacilli are capable of remaining latent for some time.

It is a different question how long one of the described forms of chronic tuberculosis of lymph nodes of slow, successive development may remain latent before death occurs from secondary tuberculosis of other organs, or accidentally from other causes. Recently Lubarsch[1] on the basis of personal observations has come to the conclusion that a clinical latency for 10 years or more of tuberculous foci is possible. With my observations in view I must place the limit considerably higher. The clinical data in certain of our cases point to a latency of 13–14–15 years (see Nos. 1, 3, 4, and 110, '00), of 28–29 years (No. 2, and a case not narrated), in one case to one of even longer duration.

The duration of latency in such forms of tuberculosis, therefore, may safely be placed at 20–30 years, and probably may be considerably longer. The term latency is used so as to comprise both cases of well encapsulated old tuberculous foci (virulent or non-virulent) in lymph nodes and the not less important latent chronic affections of lymph nodes in which the tuberculosis has made its way from one place to another in the course of many years. And I do not consider whether in these chronic affections of lymph nodes death is caused by complications brought about by them[2] or whether the affection remains latent the whole time and death is brought about by other causes. It is worthy of note and clearly brought out by the clinical histories that the infection in these cases of chronic tuberculosis of lymph nodes often dates far back in childhood; a history of enlarged nodes in childhood with repeated operations is continually obtained.

It has been shown in numerous clinical and pathological works

[1] *Loc. cit.*

[2] See the case described of complicating compression of the duodenum with secondary dilatation of the stomach.

(as the extensive work of C. Sternberg)[1] that the course of lymphatic tuberculosis may take on various forms. Certain cases do not take a latent course, but a peculiar clinical picture may be produced, characterized by a prolonged febrile condition and increasing anemia. Clinically such cases often will pass under the name of pseudoleukemia and the real cause of the disease will not be cleared up before the autopsy. It appears that these peculiarities are seen particularly in cases of rapid course showing at the same time marked breaking-down of the degenerated lymph nodes (very virulent and numerous bacilli). Among our cases showing a peculiar course are Nos. 4, 8, 10 (with a very peculiar and rare form of cutaneous tuberculosis), and particularly Case 7 which is a type of such febrile affections often of very uncertain diagnosis. I do not propose now to enter further into this highly interesting chapter as it is chiefly of clinical interest.

The localization to be considered next is primary tuberculosis of the intestine and the lymph nodes belonging to it. In order to get a view of the frequency of tuberculosis of the digestive tract in general I shall add the cases of primary tuberculosis of the faucial tonsils and cervical lymph nodes which have been discussed already in part.

Case 1. (98, '01.) A woman, 25 years old, had suffered for several years from severe attacks of epigastric pain and vomiting. She steadily lost in flesh and died of peritonitis. The autopsy revealed numerous large tuberculous ulcers throughout the small and large intestine, with perforation of one ulcer into the peritoneal cavity. In the mesentery and retroperitoneal tissue were fist-sized clusters of swollen caseous lymph nodes. From the abdomen the enlargement and caseation could be followed upwards in the mediastinum, and farther upwards along the neck, as well as to the hilus of the lungs and outwards along the bronchi. A caseous bronchial node had perforated a small bronchus and set up a tuberculous bronchopneumonia.

In this case tuberculosis of the intestine and abdominal nodes must be considered primary.

Case 2. (192, '01.) A girl, 23 years old, was taken with dyspepsia and diarrhea in April; after an acute enteritis she had lived mainly on milk but had to stop this as it turned out that the milk was "bad" and came from a cow with diseased udder. The diarrhea persisted; she steadily grew thinner and cachectic and died October 13. The autopsy revealed a marked old

[1] *Ztschr. f. Heilkunde*, 1900, 19, p. 21.

tuberculosis of the lower ileum and of the large intestine (in the process of healing and constriction). Extensive tuberculosis of the mesenteric and retroperitoneal lymph nodes. Also a tuberculous affection of the apices of both lungs; in the left apex only a few small caseous and pultaceous foci; in the right apex a larger similar focus. The hilus and posterior mediastinal nodes were tuberculous, almond-sized, decreasing in size upwards; cervical nodes and one tonsil tuberculous.

In view of the extent and age of the intestinal affection, it seems reasonable to consider it primary.

Case 3. (35, '02.) Man, aged 35, who had suffered from dyspepsia since the age of 17 years. In February, 1900, pericarditis developed, and in the summer of the same year tuberculous peritonitis; he died February 14, 1902, greatly emaciated. The autopsy revealed large caseous tuberculous nodes along the trachea and isolated ones in the neck. Inveterate tuberculous pleuritis, pericarditis, and peritonitis. Numerous tuberculous intestinal ulcers and tuberculosis of the mesenteric nodes. Lungs uninvolved.

At all events a primary intestinal tuberculosis must have existed in this case; whether the entire lymph node affection, especially that of the tracheal and hilus nodes, was secondary or due to another (and older) tuberculous infection, cannot be decided.

Case 4. Man, 25 years old, who suffered for some years from tuberculous peritonitis. There was tuberculosis of the intestines and mesenteric nodes in addition to the peritonitis, but normal lungs.

Case 5. A woman, 37 years old, had been ailing for years, especially since her last pregnancy seven years before, and had suffered from abdominal pain and dyspeptic symptoms. She died from perforative peritonitis. The autopsy revealed old tuberculous ulcers in the small and large intestine; one of the ulcers had perforated; there were adhesions and strictures. Also unilateral tuberculous salpingitis; and an old and very extensive tuberculosis with pronounced caseous and pultaceous degeneration of the lymph nodes, viz., retroperitoneal, mesenteric (most marked), iliac, inguinal, and a continuous chain in the posterior mediastinum, along the trachea, in the pulmonary hilus and on the left side of the neck. No trace of pulmonary tuberculosis.

We have here an old primary tuberculosis of the intestines and mesenteric nodes; the affection of the thoracic nodes appears to be secondary.

Case 6. (65, '03.) A man, 37 years old, died of empyema pleurae. The autopsy revealed an old left-sided tuberculous empyema. In the apex of the right lung a few tubercles and a pultaceous focus the size of a grain of maize. Large caseous lymph nodes on both sides of the neck, in the posterior mediastinum and pulmonary hila; tuberculous ulcers in the intestines, and beginning tuberculous peritonitis.

The affection of the lymph nodes and intestine is the oldest;

that of the lung was slight, looked more recent, and was completely encapsulated. The affection of the lymph nodes must be looked upon as independent of that of the intestine (descending from the neck?).

To these six cases of primary tuberculosis of the intestinal tract must be added two which were not narrated, and eight cases of primary tuberculosis of the abdominal nodes, mainly mesenteric and retroperitoneal (in one case the nodes in the groins and mesocolon). In order to include all cases of primary infection through the digestive tract, however, it is necessary further to include the three cases of extensive lymph node disease already recorded, in which infection had occurred through the throat or intestine, or both; six of the cases of general infection where the throat was considered the place of invasion, and five cases in which was assumed a primary infection through the intestinal tract partly associated with infection through the respiratory tract. Some of the latter cases, however, were somewhat doubtful. But I will not include other and not uncommon cases of extensive lymph node tuberculosis of probable origin in the abdomen or cervical nodes, and associated with tuberculosis of other internal organs, especially the lungs, which renders difficult the analysis of any single case.

We thus altogether have about 30 cases of certain or, in a few cases, very probable primary tuberculosis of the digestive tract, *i. e.*, 5.5 per cent of the total number of autopsies or 7.7 per cent of all tuberculous cases. As also most of these cases, viz., 22, directly or indirectly led to death from tuberculosis, it is of interest to compare fatal cases of this class with the total number of deaths from tuberculosis, which was 124. The percentage then is 18. This is the highest figure reached; but several cases have been omitted in which the postmortem findings were too intricate and the data too scant to admit of any definite conclusion.

In comparison it may be stated that Hof (*loc. cit.*), in considering all autopsies on tuberculous adults, found 5.9 per cent of primary infection through the digestive tract (2.3 per cent of all adults, while in 84.9 per cent of the cases infection was through the respiratory tract. Zahn found primary tuberculosis of the

digestive tract in 2.4 per cent, v. Hansemann in 3.5 per cent By including the autopsies in children, Lubarsch (*loc. cit.*) reached 5.5 per cent, and by also including tuberculosis of the tonsils, 6.3 per cent.

Primary localizations of tuberculosis, outside the respiratory and digestive tracts and lymph nodes, are not numerous. We shall only mention that they were observed as follows:

Eleven cases of bone- and joint-tuberculosis, six of which possibly were secondary, mainly to affections of the lung.

Eight cases of genito-urinary tuberculosis (six of these probably secondary).

One case of primary tuberculosis of serous membranes.

Two cases of primary tuberculosis in spleen and pancreas.

On account of the rarity the two latter cases are related:

1) 153, '02. In a man, 46 years old, who died of diabetes mellitus, and in whom there was no trace of tuberculosis in the lungs, intestinal tract, or lymph nodes, a pea-sized, rather firm nodule was demonstrated in the pancreas, which on microscopic examination was seen to consist of conglomerate tubercles.

2) At a legal autopsy in a woman, 32 years old, who had died of carbon monoxide poisoning, the spleen was found enlarged (weight, 170 g.); throughout it were numerous pea-sized yellowish-white nodules, which consisted of degenerated tissue. Microscopically the nodules were seen to consist of fibrous and hyaline tubercles, in which a few tubercle bacilli were found. No trace of tuberculosis in the rest of the body (particularly not in the lungs, intestines, or lymph nodes).

Otherwise, in the bulk of the cases, both those of fatal tuberculosis and the much more numerous ones of latent and obsolete tuberculosis, the localization was in the lungs and thoracic nodes which probably most frequently had been primarily infected.

It now remains to consider somewhat the most common of all localizations in adults, namely, pulmonary tuberculosis, especially in its connection with other tuberculous affections, and first of all with the frequent affections of lymph nodes. When at the same time tuberculous processes are found in other internal organs and first or all in the lymph nodes, one is prone to conclude that the pulmonary affection is primary; and from sputum containing tubercle bacilli tonsils and cervical nodes as well as intestines and mesenteric nodes may be secondarily infected. The question is

whether, as a rule, this is the case, or if not, the pulmonary disease may be secondary, as we frequently had to assume in our study of tuberculosis in children.

That this really may be the case will appear from a study of the cases which have been related. It has been shown that in adults as well as in children perforation into the bronchi from tuberculous nodes may take place and set up a local pulmonary tuberculosis; further, that tuberculous nodes may become adherent to the lung tissue and thus infect it. In these cases, as well as when the lung tissue is attacked by lymphogenous infection (from infected hilus or bronchial nodes, which is not of rare occurrence), we are dealing with involvement of the lungs from neighboring tuberculous organs, mainly lymph nodes. This source of pulmonary tuberculosis is also commonly recognized, though as a rule no great importance is attached to it.

The principal question, however, is whether hematogenous infection of the lungs by tubercle bacilli from some tuberculous focus may occur (either directly or indirectly after first passing through lymphatic channels). In other words, whether pulmonary tuberculosis in adults cannot be traced back to a tuberculous affection which existed at a remote time, perhaps in childhood, and which cannot be brought into direct relationship with the pulmonary lesions in any of the ways described. Old tuberculosis of lymph nodes, first of all, would then receive attention. It is needless to say that in all such considerations the possibility of a new infection (as by inhalation) must not be lost sight of.

It is this mode of infection which in late years has given rise to much animated discussion, especially in Germany. Among pathologists, Ribbert[1] in particular has come out strongly in its favor and thereby called forth most of the other works on the subject. Of later date we have the various well-known addresses by v. Behring[2] to the effect that infection with tubercle bacilli takes place in early childhood, and that subsequent pulmonary tuberculosis is traceable to it. According to this theory, for

[1] *Ueber die Ausbreitung der Tuberculose*, Marburg, 1900; *Deutsche med. Wchnschr.*, 1902, 28, p. 301, and 1904, 30, p. 300.

[2] *Deutsche med. Wchnschr.*, 1903, 29, p. 689; 1904, 30, p. 193; *Tuberculoseentstehung, Tuberculose bekämpfung und Säuglingsernährung*, 1904.

which v. Behring himself could not furnish much evidence, the lungs in all probability must be thought to be infected by way of the blood.[1] Similar views have been brought forward for some time from clinical observations, chiefly by Volland,[2] and from statistical considerations by Antvord.[3]

Ribbert derives his arguments chiefly from a consideration of miliary tuberculosis which he finds may show every transition to ordinary pulmonary tuberculosis, and he points to the frequent presence of older tuberculous changes which it appears reasonable to connect with a fresh pulmonary tuberculosis of more recent origin. He does not, however, deny an aërogenous pulmonary tuberculosis, but claims this to be a comparatively rare form, as he cannot recognize the force of the arguments brought forward in favor of frequent inhalation of tubercle bacilli. Ribbert's hypothesis in the main has been accepted by v. Baumgarten and some others, but has also met with strong opposition, especially from Cornet, and particularly Schmorl.[4] The latter has taken the matter up in its entirety and made use of the abundant material of the Pathological Institute of Dresden. His result is that the possibility af the hematogenous origin of pulmonary tuberculosis cannot be denied, but that most cases are attributable to air-borne infection. He offers as proof the fact that the oldest lesions generally are found in the lungs (the lymph nodes may even be entirely free from tuberculosis), that the hematogenous eruption in the lungs has its principal seat not at all in the apices, and finally, that in small isolated nodules in the lungs it is often possible to demonstrate directly that the mucous membrane of the small bronchi have been primarily attacked (as had previously been shown by Birch-Hirschfeld).

In regard to this whole matter I must confine myself to accentuating certain points based on personal experience. In the first place I must agree to what has first been emphasized by Orth

[1] However, v. Behring has modified his views so much that he now to some extent seems to believe that infantile tuberculosis only creates a susceptibility to a later new infection, eventually of the lungs, and by another route, such as inhalation.

[2] *Ztschr. f. klin. Med.*, 1893, 23, p. 50; *Münch. med. Wchnschr.*, 1904, 51, p. 879.

[3] *Norsk Mag. f. Laegevid.*, 1895, 4 R, 10, p. 1013; and 1898, 4 R, 13, p. 337

[4] *Münch. med. Wchnschr.*, 1902, 49, p. 1379.

and later by Ribbert, viz., that miliary tubercles (by hematogenous infection) frequently are found to be most numerous and largest in the apices, and that, chiefly in young persons, cases occasionally are met with in which it is a matter of grave doubt whether the pulmonary tuberculosis is of aërogenous or hematogenous origin (apparent transitional forms). Likewise I must maintain, with Ribbert and Orth, that pulmonary tuberculosis of hematogenous origin in its further course conducts itself like the forms commonly considered due to inhalation.

I must further emphasize that in adults, in addition to slight, well limited, and apparently recent pulmonary tuberculosis, one also finds in other organs tuberculous changes which are extensive and plainly of older date; these are chiefly in the lymph nodes, but also elsewhere, as in bones, intestinal tract, genitalia, etc.

It is therefore natural to suppose that in such cases the lungs have been secondarily infected by way of the blood (directly or indirectly) from the older tuberculous foci, for instance in the lymph nodes. This seems the more reasonable when at the same time scattered tubercles are found in other organs which must be due to hematogenous infection. But naturally, in the given case one cannot exclude the possibility of two infections having occurred, the later by inhalation. In that case it might be supposed that the old tuberculosis of the other organs had brought about increased susceptibility to a subsequent new infection. This latter explanation appears most probable in case there is a history of lymph node tuberculosis in childhood of which no trace remains, of a healed bone tuberculosis, etc.

If, however, we are dealing with a chronic progressive lymph node tuberculosis which the clinical history also shows to have existed for years, then hematogenous infection of the lungs appears to be most plausible, especially when only small recent foci are found. If the lungs at the same time are the seat of a scar, an encapsulated caseous mass, calcareous deposits, etc., no conclusions as a rule can be drawn in regard to this point.

Considerable material elucidating this question may be gathered from my cases (see the summaries). Here I shall touch only certain points.

For instance, the clinical history in cases of tuberculosis in adults often tells us that the patient had enlarged lymph nodes in childhood. This statement was made in not less than five of the cases of general lymph node tuberculosis and in one case of tuberculosis of the retroperitoneal nodes, and is of course of the greatest importance in the determination of the point of origin. Similar statements are strikingly rare in the case of the other autopsies during this period. When at autopsy no trace of tuberculous nodes or only scars or small encapsulated caseous foci are found in the neck then it must be considered very doubtful whether the pulmonary tuberculosis which later caused death had any connection whatever with the enlarged nodes which existed in childhood.

The cause of the relative rarity of a history of enlarged nodes in childhood must largely be sought in defective anamneses. For comparison it may be stated that Dr. Frich[1] who collected and elaborated the 354 cases of pulmonary tuberculosis admitted to one of the medical wards of the hospital in the course of ten years found that in 36 cases (10.4 per cent) enlarged nodes had existed.

In cases also of primary tuberculosis of other organs than the lymph nodes small recent foci of tuberculous inflammation in the lungs were not seldom found, for instance, in some of the cases of primary tuberculosis of the intestinal tract. Here also it seems probable that the pulmonary tuberculosis was secondary and hematogenous. It will always be a question of personal judgment how much to include in this regard. On studying the records of the cases of fatal pulmonary tuberculosis I should assume that at least 15–20 per cent with greater or less probability must be looked upon as secondary, and of probable hematogenous origin; cases of primary tuberculosis of the thoracic nodes are included.

But the great mass of cases of tuberculosis of the respiratory tract, both the fatal and even more the latent and obsolete ones, do not appear to have any connection with older tuberculosis lesions in other organs so far as can be determined by the post-

[1] *Norsk Mag. f. Laegevid.*, 1904, 65, p. 782.

mortem findings and the generally scant clinical data. However, I have no doubt that this proportion of 15–20 per cent would be considerably increased if further careful investigations were made, especially clinically, with the view to establishing the previous existence of tuberculosis of lymph nodes, and not only of primary infection of the thoracic nodes but also, of what has been given too little attention, descending cervical or ascending abdominal lymph node tuberculosis.

The idea of the importance of old lymph node tuberculosis in connection with the later development of ordinary pulmonary tuberculosis also receives a support in statistical works on the frequent occurrence of tuberculous nodes in childhood and of scrofulosis in general.

In our Norwegian medical literature such a connection has been maintained by Antvord chiefly[1] who holds that in as many as two-thirds of all cases of tuberculosis infection occurred in childhood. He believes that at least one-fourth of all adult consumptives were scrofulous as children. As tuberculosis in children most frequently is found in the lungs and bronchial nodes then, according to Antvord, the original infection was most likely aërogenous. He does not say in what manner pulmonary tuberculosis should arise in adults who were scrofulous in childhood; probably, however, this must be thought to occur, at least in part, by way of the blood. He does not mention new infection in adults as an explanation, and believes the study of tuberculosis in childhood will give hope of finding the real source of infection.

As has been mentioned, Volland in several articles has advocated similar views. He also believes infection to take place in early childhood, or even infancy, and mainly through the mucous membranes of the throat and nose, and through the skin, from dirt. From the lymph nodes the tubercle bacilli enter the blood and reach the apices of the lungs, where secondary tuberculosis develops. Volland leaves a new infection out of consideration.

The articles of Laser and Randers, in which also the frequency of tuberculosis of the cervical nodes in children has been emphasized, have already been mentioned.

[1] *Loc. cit.*

The importance of a preceding scrofula seems to be still clearer brought out by experience obtained at hospitals for scrofulous patients whose further fate has been followed. This is shown by the records given by Dr. Schepellern from the hospital at Refsnæs in Denmark.[1] Of 814 discharged scrofulous children, 155, or 19 per cent, were dead 10 years after discharge, and 18 per cent died of tuberculosis. Of the remaining 81 per cent, 167, or 21 per cent, still were scrofulous, and 50 of these had developed pulmonary tuberculosis. If cure is not obtained, the condition gradually passes into consumption, and this is the more common the older the person becomes. After 10 years one-third had either died of tuberculosis or were suffering from it.

German works on lymph node tuberculosis show similar results. As an instance I may mention the work of Blos[2] on tuberculous lymphomas and their relation to pulmonary tuberculosis. It treats of the children with tuberculous lymph nodes (cervical in 89 per cent) treated in Czerny's clinic in Heidelberg. Of 160 operated on at least three years previously, 26 per cent had developed tuberculosis of the lungs and 14 per cent tuberculosis of other organs. Blos also compared similar observations from other surgical clinics. The percentage of operated scrofulous children who later developed pulmonary tuberculosis varied from 10 and 11 to 22 and 26 per cent.

These observations are substantiated by many of the cases described by me, and everything is strongly in favor of pulmonary tuberculosis being secondary (by hematogenous infection) in a not small proportion of cases.

As the result of these considerations, I must maintain that also in adults pulmonary tuberculosis may be and often is secondary. The cause is then to be sought in tuberculous foci in other organs, but mainly in the lymph nodes, and the infection of the lungs occurs most likely by way of the blood (from the thoracic nodes the infection might also easily occur through the lymphatics). I hope in the numerous cases recorded to have furnished anatomic support for such a view. With my obser-

[1] Cited from Antvord's article in 1898.

[2] *Mittheil. aus den Grenzgeb. d. Med. u. Chir.*, 1899, 4, p. 520.

vations in mind (including the latent bacilli in children), I also believe I may maintain that much more stress must be laid upon primary infection through the digestive tract, and not least on infection through the throat, than has been done formerly. Clinical experience also points in the same direction.

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